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Prednisolone Versus Dexamethasone for Croup: a Randomized Controlled Trial

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abstract

OBJECTIVES: The use of either prednisolone or low-dose dexamethasone in the treatment of childhood croup lacks a rigorous evidence base despite widespread use. In this study, we compare dexamethasone at 0.6 mg/kg with both low-dose dexamethasone at 0.15 mg/kg and prednisolone at 1 mg/kg.

METHODS: Prospective, double-blind, noninferiority randomized controlled trial based in 1 tertiary pediatric emergency department and 1 urban district emergency department in Perth, Western Australia. Inclusions were age >6 months, maximum weight 20 kg, contactable by telephone, and English-speaking caregivers. Exclusion criteria were known prednisolone or dexamethasone allergy, immunosuppressive disease or treatment, steroid therapy or enrollment in the study within the previous 14 days, and a high clinical suspicion of an alternative diagnosis. A total of 1252 participants were enrolled and randomly assigned to receive dexamethasone (0.6 mg/kg; $n = 410$), low-dose dexamethasone (0.15 mg/kg; $n = 410$), or prednisolone (1 mg/kg; $n = 411$). Primary outcome measures included Westley Croup Score 1-hour after treatment and unscheduled medical re-attendance during the 7 days after treatment.

RESULTS: Mean Westley Croup Score at baseline was 1.4 for dexamethasone, 1.5 for low-dose dexamethasone, and 1.5 for prednisolone. Adjusted difference in scores at 1 hour, compared with dexamethasone, was 0.03 (95% confidence interval −0.09 to 0.15) for low-dose dexamethasone and 0.05 (95% confidence interval −0.07 to 0.17) for prednisolone. Re-attendance rates were 17.8% for dexamethasone, 19.5% for low-dose dexamethasone, and 21.7% for prednisolone (not significant [$P = .59$ and .19]).

CONCLUSIONS: Noninferiority was demonstrated for both low-dose dexamethasone and prednisolone. The type of oral steroid seems to have no clinically significant impact on efficacy, both acutely and during the week after treatment.

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Dr Parker conceptualized and designed the study, coordinated and supervised data collection, drafted the initial manuscript, and reviewed and revised the manuscript; Dr Cooper performed the statistical analysis of the data and reviewed and revised the manuscript; and both authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

This trial has been registered with the Australian New Zealand Clinical Trials Registry (https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id = 83722) (identifier ACTRN12609000290291).

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WHAT'S KNOWN ON THIS SUBJECT: Although dexamethasone at 0.6 mg/kg is an established evidence-based treatment of childhood croup (reducing hospital admissions, length of stay, and need for endotracheal intubation), alternative corticosteroid regimes are in widespread use based on evidence from small studies and observational data.

WHAT THIS STUDY ADDS: With our study, we confirm that prednisolone at 1 mg/kg and dexamethasone at 0.15 mg/kg are both noninferior to dexamethasone at 0.6 mg/kg for the treatment of croup in children. We found no difference between groups for both acute croup severity and unscheduled medical re-attendance after treatment.

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The efficacy and safety of corticosteroids for the treatment of croup has established their use as routine therapy for the emergency department (ED) management of croup,[1–3] including, at our own institution, all ED attendances for croup.[4] Steroid treatments have been shown to significantly decrease the rate of hospital admission, length of hospital stay, return visits, endotracheal intubation, and admission to ICUs in patients with croup.[5–9] Although different routes of corticosteroid administration have been used, including nebulized, intramuscular, and intravenous dosing, the oral route has many advantages and is the preferred route in many centers.[10,11] The clinician treating children with croup may further consider the type and dose of oral steroid.

Although early trials revealed safety and efficacy with intramuscular dexamethasone at a dose of 0.6 mg/kg,[6] subsequent studies revealed efficacy of oral dexamethasone,[7] and there is evidence that smaller doses of dexamethasone (0.3 and 0.15 mg/kg po) may be equally efficacious.[12] The lower oral dose of 0.15 mg/kg has been accepted and implemented in some centers[2]; however, the limited number of supporting studies[7,12] raises the question of efficacy compared with a dose of 0.6 mg/kg po,[9,13] particularly around the power of these studies to detect small, but clinically important, differences in outcomes. Notably, the studies by Geelhoed and Macdonald[12] had only 80% power (at the 5% significance level) to detect a doubling in the duration of hospitalization, which would only reveal a relatively large clinical difference between treatments. On the other hand, the lower dose is supported by almost 3 decades of clinical experience at our institution, indicating no rise in the rate of intubation or admission to intensive care after a reduction of the dose to 0.15 mg/kg po.[4] The well-proven efficacy of prednisolone in a dose of 1 mg/kg po for croup in patients receiving intubation[14] suggests that a comparable glucocorticoid dose of dexamethasone (~0.15 mg/kg) should be equally effective.[15]

Prednisolone (1 mg/kg) has been shown in 1 study to shorten the time to extubation for patients with croup in intensive care.[14] Many centers therefore use oral prednisolone for the ED management of croup as a more readily available alternative to dexamethasone.[16] The type and dose of corticosteroid treatment of croup depends largely on geographic location because different centers preferentially administer different drugs and doses. There have only been 3 small randomized controlled trials used to compare oral dexamethasone with oral prednisolone. Fifoot and Ting[16] found no difference between the 2 treatments, and an earlier study by Sparrow and Geelhoed[17] of 133 children with mild to moderate croup revealed that children treated with prednisolone (1 mg/kg po) were more likely to seek unscheduled follow-up for medical care than children treated with dexamethasone (0.15 mg/kg po). Garbutt et al[18] found no difference in duration of croup symptoms or additional health care when comparing a single dose of dexamethasone with 3 days of prednisolone treatment.

In this study, we aim to compare the traditional, evidence-supported gold standard croup treatment, dexamethasone at a dose of 0.6 mg/kg, with 2 alternate treatments already in widespread use, namely lower-dose dexamethasone (0.15 mg/kg) and prednisolone (1 mg/kg), and assess these treatments for noninferiority.

METHODS

Design

We conducted a prospective, double-blind, randomized controlled trial at 2 urban EDs: Princess Margaret Hospital for Children (a tertiary pediatric center) and Joondalup Health Campus (an urban district hospital). Hospital research ethics committee approval was obtained at both centers, and the study was registered with the Australian New Zealand Clinical Trials Registry (identifier ACTRN12609000290291). De-identified individual participant data will not be made available.

Participants

Patients were a convenience sample of children presenting to either of the EDs with croup during the study period (March 2009–July 2012). The disease state was defined as a clinical diagnosis of croup (laryngotracheitis) by the ED doctor after a history and physical examination. If there was any diagnostic uncertainty, clinicians could refer to a Guidance for Doctors information sheet (Supplemental Information), in which a croup diagnosis is defined as a hoarse voice or barking cough and stridor (with or without increased work of breathing) directly observed or elicited in the history. Inclusion criteria were age >6 months, contactable by telephone, and English-speaking caregivers. A maximum weight of 20 kg was imposed to limit the maximum possible dexamethasone dose to 12 mg (adult dose). Exclusion criteria included known prednisolone or dexamethasone allergy, immunosuppressive disease or treatment, steroid therapy or enrollment in the same study within the previous 14 days, and a high clinical suspicion of an alternative diagnosis, with specific prompts to include bacterial tracheitis, inhaled foreign body, retropharyngeal abscess, epiglottitis, angioedema, vascular ring, and subglottic stenosis. Signed consent was obtained from caregivers by the treating doctor after the doctor provided a standardized information sheet (Croup Study: Information for Parents, see Supplemental Information).

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Interventions

Patients were randomly assigned to 1 of 3 interventions: dexamethasone (0.6 mg/kg; standard "control" treatment), low-dose dexamethasone (0.15 mg/kg), or prednisolone (1 mg/kg). The randomization list was computer-generated at www.randomization.com by using randomly permuted block sizes in the ratio of 4 patients from each group, with block randomization by center. All medications were prepared, randomly assigned, and labeled by a clinical trials pharmacist at Princess Margaret Hospital. To preserve the influence of palatability, no masking agents were used; however, individual doses of the trial medication were identically packaged, dispensed via a dispensing rack in order of randomization, and dosed at 0.3 mL/kg by the nurse after enrollment and initial severity scoring. Both staff (administering and assessing treatments) and patients were therefore blinded to the treatment allocation.

Outcomes

The study had 2 primary outcome measures: (1) an objective and validated[3,19] measure of croup severity, the Westley Croup Score (WCS),[20] and (2) re-attendance for follow-up of ongoing symptoms.

The WCS is a clinical croup score, with a range of 0 to 17 points, that is based on stridor, retractions, air entry, cyanosis, and level of consciousness (Supplemental Fig 5). It is possible to have a clinical diagnosis of croup that is based on a history of a barking cough and yet have a WCS of 0, with no stridor or retractions and normal air entry. The WCS was assessed at baseline, at 1 hour after treatment, hourly up to 6 hours, and again at 12 hours for patients not yet discharged from the hospital; patients were discharged when clinically appropriate (Croup Oral Steroid Study: Guidance for Doctors, see Supplemental Information). The second primary outcome was unscheduled medical re-attendance (for any reason) during the 7 days after treatment. This information was obtained via a telephone call to caregivers within 4 weeks after discharge. If the caregiver was deemed as not contactable (after several failed contact attempts), re-attendance to the ED with a diagnosis of croup was searched for electronically.

Secondary outcomes included total hospital stay, ED length of stay, vomiting, use of nebulized epinephrine (adrenaline), endotracheal intubation, need for additional steroid doses, and need for admission to an inpatient ward, emergency short-stay unit, or ICU.

Statistical Analysis

The study was designed to demonstrate the noninferiority[21] of low-dose dexamethasone and prednisolone relative to the standard full dose of dexamethasone for the 2 primary outcomes: (1) WCS (from baseline) at 1 hour and subsequent hourly intervals after administration and (2) the rate of unscheduled medical re-attendance in the 7 days after administration. The analysis was conducted per protocol via intention to treat; noninferiority was specified as the upper bound of the 2-sided 95% confidence interval (CI) for the reduction in WCS (for the intervention group [low-dose dexamethasone or prednisolone] relative to the standard treatment group [dexamethasone]) not exceeding 0.5. Whereas authors of some previous studies have used a WCS of 1 as a clinically important difference,[22] we selected 0.5 to increase the study's discriminatory ability[21] among milder croup cases (scores between 0 and 2), which typically account for the majority of patients.[3] Under this design, it was determined that 437 participants would be required, per arm, to provide 90% power to demonstrate noninferiority (by using a 2-sided *t* test; common SD of 1.8; $\alpha = .05$). The expected re-attendance rate for croup at our institution is 4% to 6%[4]; this sample size would provide 85% power to detect an absolute difference in re-attendance rate of 5% (based on 10% vs 5%; $\alpha = .05$).

Descriptive statistics are presented as mean and SD, median, or count and percentage, as appropriate. A per-protocol analysis was used to employ linear regression, adjusted for baseline levels, of the postadministration hourly assessment of the WCS to calculate 95% CIs for the difference between groups. The χ^2 test was used to compare the frequency of dichotomous and categorical variables; a 1-way analysis of variance or Student's *t* test was used to compare parametric variables, either between all groups or between each intervention group and the control group, respectively. Secondary outcomes were analyzed by using the same techniques; because of a moderate right skew, length of stay was analyzed after a log transformation, and the ratio of geometric means between groups is reported. For patients whose WCS was not recorded at an hourly assessment, if, and only if, their baseline WCS was 0 and they were discharged within the 60 minutes preceding that assessment, their score was assumed to be 0 for that assessment. Post hoc consistency analyses included additional modeling approaches to validate the per-protocol analysis. This included dichotomizing patients according to their status of recovered (either discharged or with a WCS of 0 at the hourly clinical review [assuming it was not 0 at baseline]) versus not recovered (still within the hospital) or improved (either discharged or with a WCS lower at the hourly clinical review than at baseline) versus not improved (still within the hospital) and using logistic regression

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to generate odds ratios (ORs) and 95% CIs for each treatment relative to the control group. The WCS at the hourly clinical review was also analyzed unmodified via ordinal logistic regression to generate ORs with 95% CIs. Models were adjusted for age and study center and, when appropriate, baseline WCS. Because of the higher than anticipated number of patients with multiple attendances within the study, post hoc analyses were conducted to calculate the intraclass correlation coefficient and to replicate the per-protocol analysis with clustering on subject identification. All data manipulation and analysis were conducted in R.[23]

Patient and Public Involvement

There was no patient and public involvement in the study design or implementation. No patients or their representatives were asked to help interpret or disseminate the results.

RESULTS

Trial Population

A total of 1252 patient attendances underwent random assignment into the trial. After exclusions (Fig 1), 1231 patients entered the analysis set; 410 were assigned to dexamethasone (0.6 mg/kg), 410 were assigned to low-dose dexamethasone (0.15 mg/kg), and 411 assigned to prednisolone (1 mg/kg). These 1231 attendances included 105 repeat enrollments: 48 patients enrolling twice and a further 3 patients enrolling 3 times each, all outside the 14-day exclusion period. Twenty-eight patients were enrolled despite meeting ≥1 exclusion criterion; 19 children weighing >20 kg, 4 children with laryngomalacia, 4 children with steroid use in the 14 preceding days, and 3 children <6 months of age all were included in the analysis on an intention-to-treat basis. The distribution of repeat enrollments and patients meeting an exclusion criterion was relatively balanced across treatment groups (dexamethasone/low-dose dexamethasone/prednisolone distributed at 1:1.48:1.14 and 1:1.29:1.71, respectively). The mean age and weight of patients was 30 months and 14.0 kg, respectively; 38% of patients were girls, and these characteristics, in addition to croup severity at presentation (baseline WCS), did not differ between groups (Table 1).

Primary Outcomes

The percentage of patients available for the 1-hour assessment was similar between groups at 88.3%, 88.3%, and 89.1% for dexamethasone, low-dose dexamethasone, and prednisolone, respectively. There was no statistically significant difference between the 3 groups for the WCS at the 1-hour assessment, with the adjusted difference in scores at 1 hour (relative to the dexamethasone group) being 0.03 (95% CI −0.09 to 0.15) for low-dose dexamethasone and 0.05 (95% CI −0.07 to 0.17) for prednisolone (Table 2, Fig 2). The upper limits of these CIs fall within the prespecified noninferiority margin of 0.5.

Re-attendance rates (Table 2) were modest at 17.8% (dexamethasone), 19.5% (low-dose dexamethasone), and 21.7% (prednisolone), and similarly, ED re-attendance rates were low at 5.9% (dexamethasone), 8.8% (low-dose dexamethasone), and 7.5% (prednisolone), with no statistical difference between treatment groups (Table 3).

For the low-dose dexamethasone group relative to the dexamethasone group, the WCS was 0.11 higher at 2 hours and 0.23 higher at 3 hours (Fig 2); although the difference was significant at the 3-hour assessment (*P* = .04), the upper limit of the 95% CI (0.45) was within the noninferiority margin (Table 4, Fig 3). These estimates were 0.04 at 2 hours and 0.04 at 3 hours for the prednisolone group, with the upper limit of the 95% CIs not crossing 0.5. These results must be interpreted with caution given the lower numbers.

Consistency analyses for the odds of recovery (WCS of 0 or discharged) and improvement (lower WCS) are shown in Table 4, with no statistically significant differences demonstrated.

Secondary Outcomes and Adverse Events

The median length of stay across patients was 124 minutes; this did not differ significantly between the study groups (*P* = .23), as reflected in the number of patients for which hourly assessment data were available (87.4%, 12.4%, 4.2% for hours 1, 2, and 3, respectively). The ratio of geometric means for total length of stay, relative to dexamethasone, was 0.99 (95% CI 0.92 to 1.07) and 1.04 (95% CI 0.97 to 1.12) for low-dose dexamethasone and prednisolone, respectively (Fig 4). There was no difference (*P* = .63) between groups in the percentage of participants whose total length of stay exceeded 4 hours (8.8%, 7.1%, and 8.5% for dexamethasone, low-dose dexamethasone, and prednisolone, respectively). The intraclass correlation coefficient was lower for the recovery at 1 hour (0.17) but higher for length of stay (0.52); despite this, incorporation of clustering only saw changes to the SEs in the third and fourth decimal place; therefore, per-protocol analyses are presented.

There were no differences between treatment groups in the need for nebulized epinephrine (2.2%–3%) or in incidence of vomiting (up to 4%) after treatment (Table 3). A repeat dose of epinephrine was given to 0%, 1.2%, and 1.0% of participants in the dexamethasone, low-dose dexamethasone, and prednisolone groups, respectively. No study participants required intubation, and none were admitted to intensive care

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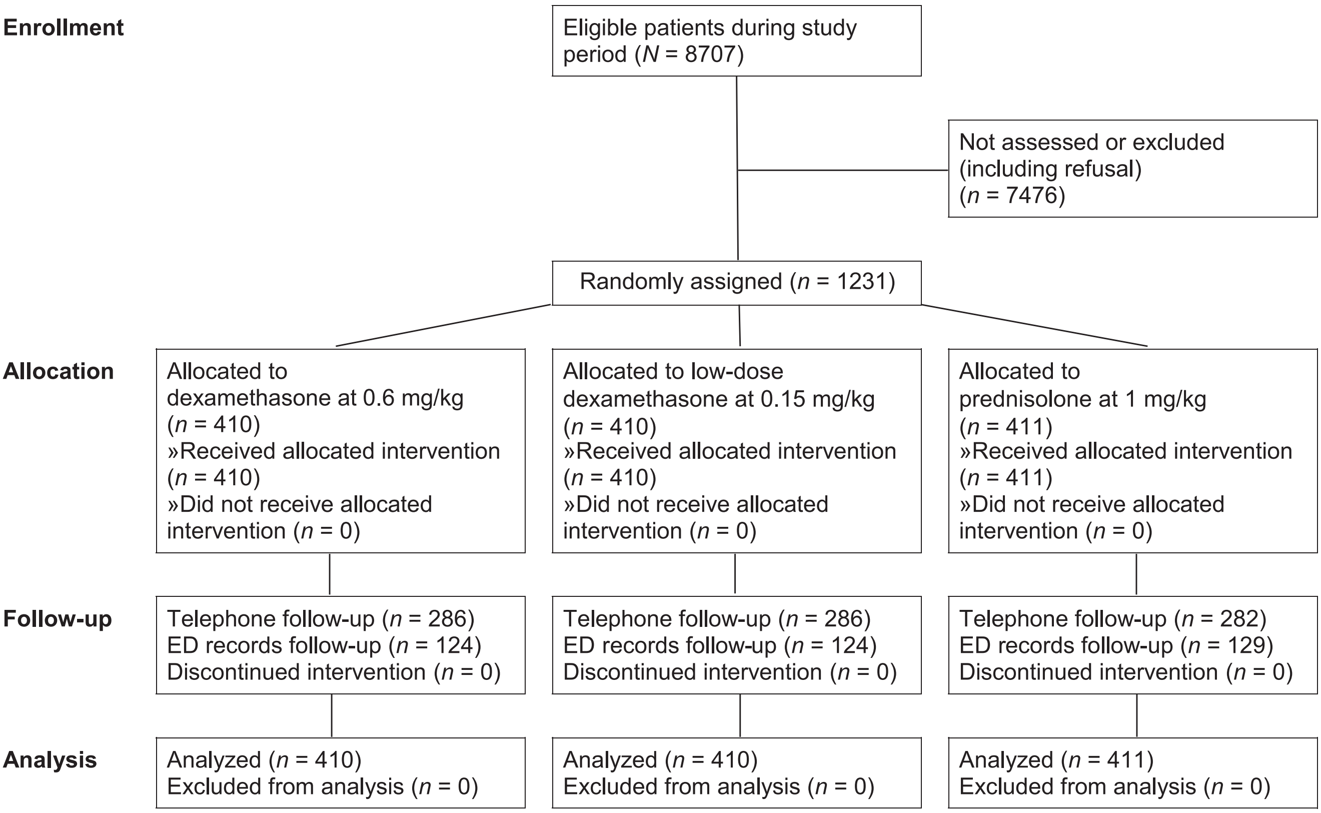
Enrollment
Eligible patients during study period (N = 8707)
Not assessed or excluded (including refusal) (n = 7476)
Randomly assigned (n = 1231)
Allocation
Allocated to dexamethasone at 0.6 mg/kg (n = 410)
»Received allocated intervention (n = 410)
»Did not receive allocated intervention (n = 0)
Allocated to low-dose dexamethasone at 0.15 mg/kg (n = 410)
»Received allocated intervention (n = 410)
»Did not receive allocated intervention (n = 0)
Allocated to prednisolone at 1 mg/kg (n = 411)
»Received allocated intervention (n = 411)
»Did not receive allocated intervention (n = 0)
Follow-up
Telephone follow-up (n = 286)
ED records follow-up (n = 124)
Discontinued intervention (n = 0)
Telephone follow-up (n = 286)
ED records follow-up (n = 124)
Discontinued intervention (n = 0)
Telephone follow-up (n = 282)
ED records follow-up (n = 129)
Discontinued intervention (n = 0)
Analysis
Analyzed (n = 410)
Excluded from analysis (n = 0)
Analyzed (n = 410)
Excluded from analysis (n = 0)
Analyzed (n = 411)
Excluded from analysis (n = 0)

FIGURE 1
Consolidated Standards of Reporting Trials diagram of flow of participants through trial stages.

during their hospitalization. One or more additional steroid doses were given to 11.3%, 15.1%, and 18.9% of participants in the dexamethasone, low-dose dexamethasone, and prednisolone groups, respectively (*P* = .04).

Adverse events were reported in only 4 patients; 1 child assigned to dexamethasone had a 30-second febrile convulsion ~30 minutes after dosing, which was not attributed to the medication by the treating clinicians; 1 child assigned to prednisolone developed insomnia (dose at ~5:00 PM and awake until 3:00 AM); 1 child assigned to low-dose dexamethasone was transferred back to the ED from the ED short-stay unit and treated with nebulized epinephrine for possible stridor; and 1 patient assigned to low-dose dexamethasone developed hyperactivity 30 minutes after the dose.

TABLE 1 Baseline Patient Characteristics, by Treatment Group

Variable	Dexamethasone (Standard Treatment)	Low-Dose Dexamethasone	Prednisolone
n	410	410	411
Demographic variables			
Age at presentation, mean (SD), mo	29.2 (17.3)	30.5 (16.3)	30.4 (16.2)
Female sex, *n* (%)	160 (39.0)	156 (38.0)	152 (37.0)
Wt, mean (SD), kg	13.8 (3.7)	14.1 (3.4)	14.0 (3.8)
Baseline characteristics			
WCS at enrollment, mean (SD)	1.4 (1.4)	1.5 (1.4)	1.5 (1.4)
WCS category at enrollment, *n* (%)			
0–1	226 (55.4)	216 (52.9)	224 (54.5)
2–3	157 (38.5)	165 (40.4)	160 (38.9)
4+	25 (6.1)	27 (6.6)	27 (6.6)

P value were calculated by using Student's *t* test for continuous outcomes and the χ^2 test for categorical outcomes.

DISCUSSION

The ToPDoG (Trial of Prednisolone/Dexamethasone Oral Glucocorticoid) study, is, to the best of our knowledge, the largest croup randomized controlled trial published to date. Our findings confirm the clinical experience of safety[24] and efficacy[1,8,9,25] of oral steroids for croup. We studied 2 different but complementary primary outcome measures: an objective measure of acute severity and improvement (the WCS) and also a real-world, clinically relevant outcome, re-attendance rate, which has implications for patient and family satisfaction as well as use of resources in hospitals and the wider community.

Dexamethasone is generally not available outside of the hospital

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TABLE 2 WCS and Re-attendance, by Treatment Group

Variable	Dexamethasone (Standard Treatment)	Low-Dose Dexamethasone	β Coefficient (95% CI)	*P*	Prednisolone	β Coefficient (95% CI)	*P*
WCS at 1 h	0.43 (0.92) (*n* = 362)	0.48 (0.95) (*n* = 362)	.03 (−0.09 to 0.15)	.62	0.49 (1.04) (*n* = 366)	.05 (−0.07 to 0.17)	.40
Change in WCS to 1 h	1.05 (1.25) (*n* = 362)	1.07 (1.25) (*n* = 362)	—	—	1.03 (1.17) (*n* = 366)	—	—
Re-attendance rate (GP and ED)	73 (17.8%)	80 (19.5%)	—	.59	89 (21.7%)	—	.19

Data are presented as mean (SD) or count (%), as appropriate. β coefficients (95% CI) represent the differences between the treatment groups and standard treatment (dexamethasone) in the WCS at the follow-up assessment and was calculated by using linear regression adjusted for age, baseline WCS, and study center. The *P* value for difference was calculated by using linear regression or the χ^2 test. —, not applicable.

environment, so there is a distinct advantage of being able to use prednisolone to treat croup in the community setting. We chose not to use masking agents in the preparation of trial medications because palatability issues affect the real-world utility of these medications, especially in pediatric populations.

A number of limitations were applicable to our study. The study population was a convenience sample from 2 institutions, and ∼1 in 7 patients with croup were enrolled. Our power calculation (based on hypothesis testing) predicted that 1311 patients were required; we only enrolled 1252 subjects. However, the CIs in our data suggest that our sample was large enough to answer the clinical questions posed.

We were unable to record the number of participants screened for inclusion, and the number of patients who were excluded or who declined consent because data collection sheets were only retained for those who met enrollment criteria. Because of limited resources and challenging logistics (general population, ED sample), follow-up was not as robust as intended, with only ∼70% of families contactable by phone. For the remaining 30%, we had to search ED attendance records for re-attenders diagnosed with croup; we were not able to assess all re-attendances in the study group; therefore, we may have missed those who re-attended ED with a different diagnosis, and we were unable to determine the rate of general practitioner (GP) re-attendance in this group.

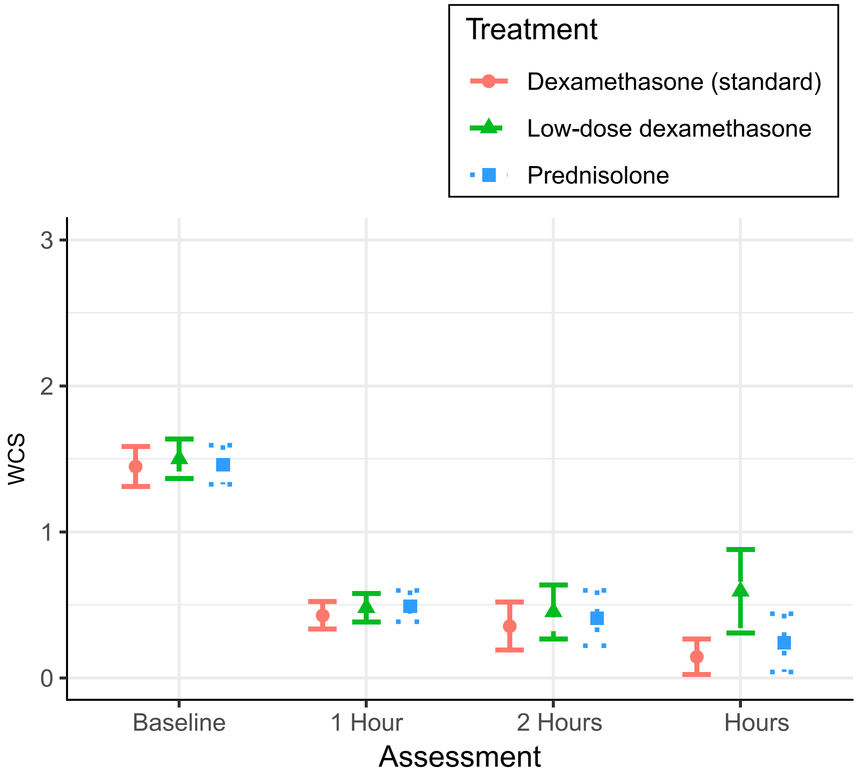

FIGURE 2
Westley Croup Score by time and treatment group. Westley Croup Score, mean and 95% confidence interval by assessment and treatment group; circle and solid line represents dexamethasone, triangle and dashed lined represents low-dose dexamethasone, and square and dotted line represents prednisolone.

Our results indicate that it is acceptable to use any of the 3 commonly used oral steroid regimes to treat croup in children. The vast majority (92%) of patients were successfully treated and discharged within 2 hours, improving from an average WCS of ∼1.5 to ∼0.5 over the first hour after treatment, with no differences between the 3 groups. The “ceiling effect” proposed by Geelhoed and Macdonald,[12] whereby steroid doses higher than a certain threshold would not have any additional benefit, seems to be applicable in these patients, in line with several decades of experience with using low-dose dexamethasone for croup at our institution.[4] Our study revealed ED re-attendance rates similar to those from other studies,[7,8,16–18] with no differences

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TABLE 3 Re-attendance, Secondary Outcomes, and Adverse Events, by Treatment Group

Variable	Dexamethasone (Standard Treatment)	Low-Dose Dexamethasone	*P*	Prednisolone	*P*
Follow-up status					
Phone call	286 (69.8%)	286 (69.8%)	1.00	282 (68.6%)	.78
ED records	124 (30.2%)	124 (30.2%)	—	129 (31.4%)	—
Re-attendance to medical care					
No further treatment sought	337	330	.25	322	.37
Attended GP	49	44	—	58	—
Re-attended ED	24	36	—	31	—
Secondary outcomes					
Nebulized epinephrine	9 (2.2%)	12 (3.0%)	.65	10 (2.5%)	.99
Endotracheal intubation	0	0	—	0	—
Admission to intensive care	0	0	—	0	—
Additional steroid dose(s)[a]	32 (11.3%)	42 (15.1%)	.22	53 (18.9%)	.02
Total length of stay, min	125	120	.36	126	.79
Length of stay >4 h	36 (8.8%)	29 (7.1%)	.44	35 (8.5%)	.99
Adverse events					
Vomiting	16 (4.0%)	13 (3.3%)	.75	13 (3.3%)	.74
Other	1	2	—	1	—

Data are presented as count (%), median, or count, as appropriate. *P* values were calculated by using the χ^2 test or, for total length of stay, by using a Kruskal-Wallis test. —, not applicable.

[a] The denominator was reduced because of missing data.

between groups for either GP or ED croup re-attendance.

When comparing the groups at 2- and 3-hour clinical reviews, there appears to be a progressive divergence of the WCS for low-dose dexamethasone compared with dexamethasone. Although this difference reached statistical significance (*P* = .042), the effect size was moderate (0.23), and even with the relatively reduced sample size available for the 3-hour clinical review, the upper limit of the CI lies within the predefined noninferiority margin of a 0.5 difference in the WCS. This result is broadly consistent with noninferiority,[21] although it is suggestive of a worse outcome for low-dose dexamethasone. One possible explanation would be that the steroid ceiling is at a dose higher than 0.15 mg/kg for a minority of patients.

Duration of treatment has been raised by some authors[18,26] who suggest that treatment with prednisolone

TABLE 4 Additional Analysis and Consistency Analysis for Change in WCS, by Treatment Group

Variable	Dexamethasone (Standard Treatment)	Low-Dose Dexamethasone	β Coefficient or OR (95% CI)	*P*	Prednisolone	β Coefficient or OR (95% CI)	*P*
WCS at 2 h	0.36 (0.86) (*n* = 107)	0.45 (1.05) (*n* = 126)	.11 (−0.08 to 0.30)	.41	0.41 (0.95) (*n* = 100)	.04 (−0.17 to 0.24)	.72
Change in WCS to 2 h	0.86 (1.42) (*n* = 107)	0.75 (1.30) (*n* = 126)	—	—	0.89 (1.27) (*n* = 100)	—	—
WCS at 3 h	0.15 (0.47) (*n* = 62)	0.59 (1.10) (*n* = 59)	.23 (0.01 to 0.45)	.04	0.24 (0.87) (*n* = 75)	.04 (−0.17 to 0.24)	.73
Change in WCS to 3 h	0.48 (1.07) (*n* = 62)	0.63 (1.26) (*n* = 59)	—	—	0.55 (1.21) (*n* = 75)	—	—
Alternative outcomes							
1 h							
Recovered	170 (44.7%)	173 (44.9%)	1.01 (0.76 to 1.34)	.97	170 (43.8%)	0.96 (0.72 to 1.27)	.77
Improved	220 (60.3%)	230 (62.7%)	1.10 (0.82 to 1.49)	.52	216 (58.9%)	0.95 (0.70 to 1.27)	.71
Ordinal outcome	—	—	1.05 (0.72 to 1.54)	.79	—	1.10 (0.75 to 1.62)	.62
2 h							
Recovered	215 (70.3%)	222 (74.0%)	1.20 (0.84 to 1.72)	.32	202 (67.8%)	0.89 (0.63 to 1.25)	.49
Improved	230 (95.8%)	239 (94.1%)	0.67 (0.29 to 1.52)	.35	220 (96.9%)	1.30 (0.49 to 3.66)	.60
Ordinal outcome	—	—	1.52 (0.76 to 3.10)	.24	—	1.00 (0.48 to 2.09)	.99

Data are presented as mean (SD) or count (%), as appropriate. β coefficients (95% CI) represent the differences between the treatment groups and standard treatment (dexamethasone) in the WCS at the follow-up assessment and were calculated by using linear regression adjusted for age, baseline WCS, and study center. ORs (95% CI) were calculated by using logistic regression (recovered and improved) or ordinal regression adjusted for age, baseline WCS (as appropriate), and study center. *P* values were calculated by using linear regression, logistic regression, or ordinal regression, in line with coefficient reporting. —, not applicable.

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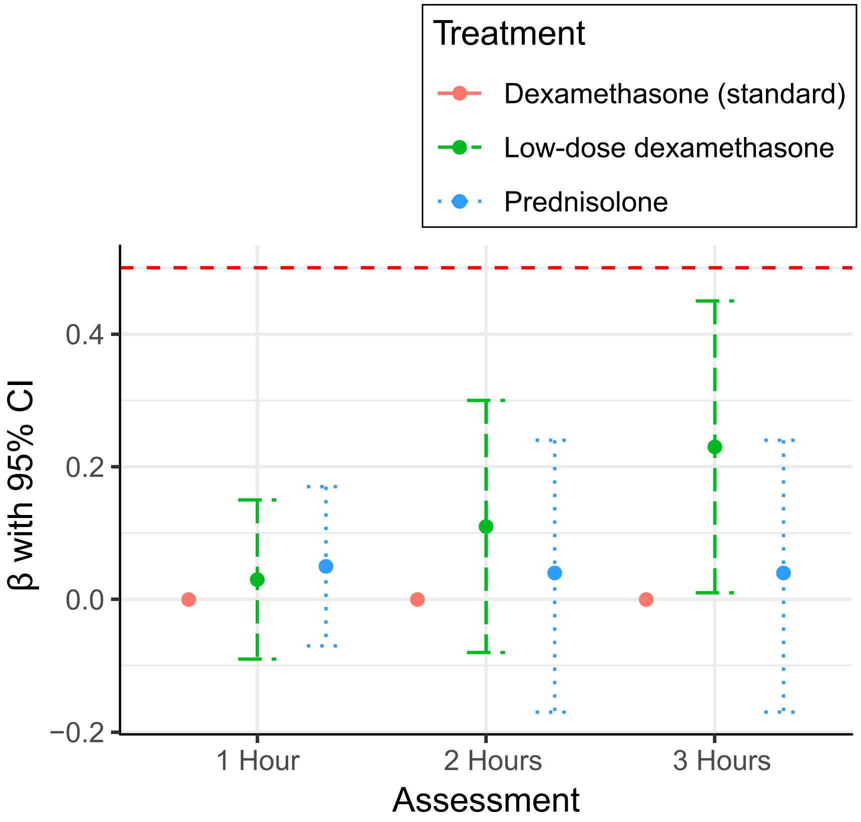

FIGURE 3
Beta coefficient for low-dose dexamethasone and prednisolone groups relative to dexamethasone for WCS at the first three hourly assessments. Point represents the estimate of the difference in WCS at follow-up assessment between treatment groups (relative to dexamethasone [standard]), calculated via linear regression adjusted for age, baseline WCS, and study center; error bars represent 95% confidence interval around the beta estimate.

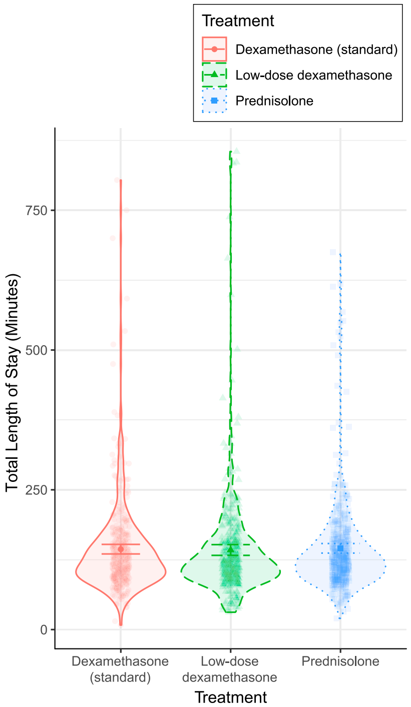

FIGURE 4
Length of stay by treatment group. Violin plot of total length of stay by treatment group; points have a horizontal jitter for separation; mean and 95% confidence interval are indicated; display data truncated to length of stay less than 1000 minutes, 9 data points were removed from dexamethasone, 3 from low-dose dexamethasone, and 5 from prednisolone.

should constitute multiple doses (3 days in the study by Garbutt et al[18]) to cover the expected duration of the illness because prednisolone has a shorter clinical duration of action.[15] Our study was not designed to test different durations of treatment, but it did reveal that patients treated with a single dose of prednisolone were statistically more likely ($P = .02$) to receive additional doses of the steroid than those treated with dexamethasone.

One suggestion for further study relates to the apparent weakening performance for low-dose dexamethasone (0.15 mg/kg) at the 3-hour assessment. This effect may be due to a small number of patients who do not respond to oral steroid treatment within 1 to 2 hours, constituting a treatment-resistant cohort; <4% of our patients were still in the ED at the 3-hour mark. These nonresponders may have different responses to steroid treatment, or they may require higher doses to effectively treat their croup.

CONCLUSIONS

Oral steroids are an effective treatment of croup, and the type of steroid seems to have no clinically significant impact on efficacy, both acutely and during the week after treatment. Children treated with prednisolone initially are more likely to require additional doses to cover the duration of the illness.

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ABBREVIATIONS

CI: confidence interval
ED: emergency department
GP: general practitioner
OR: odds ratio
WCS: Westley Croup Score

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Differences in Parent-Toddler Interactions With Electronic Versus Print Books

Tiffany G. Munzer, MD,[a] Alison L. Miller, PhD,[b,c] Heidi M. Weeks, PhD,[d] Niko Kaciroti, PhD,[c,e] Jenny Radesky, MD[a]

abstract

OBJECTIVES: Previous research has documented less dialogic interaction between parents and preschoolers during electronic-book reading versus print. Parent-toddler interactions around commercially available tablet-based books have not been described. We examined parent-toddler verbal and nonverbal interactions when reading electronic versus print books.

METHODS: We conducted a videotaped, laboratory-based, counterbalanced study of 37 parent-toddler dyads reading on 3 book formats (enhanced electronic [sound effects and/or animation], basic electronic, and print). We coded verbalizations in 10-second intervals for parents (dialogic, nondialogic, text reading, format related, negative format-related directives, and off task) and children (book related, negative, and off task). Shared positive affect and collaborative book reading were coded on a scale of 1 to 5 (5 = high). Proc Genmod and Proc Mixed analyzed within-subjects variance by book format.

RESULTS: Parents showed significantly more dialogic (print 11.9; enhanced 6.2 [$P < .001$]; basic 8.3 [$P < .001$]), text-reading (print 14.3; enhanced 10.6 [$P = .003$]; basic 14.4 [$P < .001$]), off-task (print 2.3; enhanced 1.3 [$P = .007$]), and total (29.5; enhanced 28.1 [$P = .003$]; basic 29.3 [$P = .005$]) verbalizations with print books and fewer format-related verbalizations (print 1.9; enhanced 10.0 [$P < .001$]; basic 8.3 [$P < .001$]). Toddlers showed more book-related verbalizations (print 15.0; enhanced 11.5 [$P < .001$]; basic 12.5 [$P = .005$]), total verbalizations (print 18.8; enhanced 13.8 [$P < .001$]; basic 15.3 [$P < .001$]), and higher collaboration scores (print 3.1; enhanced 2.7 [$P = .004$]; basic 2.8 [$P = .02$]) with print-book reading.

CONCLUSIONS: Parents and toddlers verbalized less with electronic books, and collaboration was lower. Future studies should examine specific aspects of tablet-book design that support parent-child interaction. Pediatricians may wish to continue promoting shared reading of print books, particularly for toddlers and younger children.

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Dr Munzer conceptualized and designed the study, coordinated and supervised data collection, drafted the initial manuscript, and reviewed and revised the manuscript; Dr Miller conceptualized and designed the study and reviewed and revised the manuscript; Dr Weeks conducted the data management, processing, and analyses and reviewed and revised the manuscript; Dr Kaciroti created the data analysis plan, conducted the data analysis, and reviewed and revised the manuscript; Dr Radesky conceptualized and designed the study, coordinated and supervised data collection, and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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WHAT'S KNOWN ON THIS SUBJECT: When preschoolers read electronic books with parents, parents may show less dialogic reading, and talk is often focused on the technology. It is not known whether toddler-parent interactions differ when reading commercially available electronic books compared with print.

WHAT THIS STUDY ADDS: Parents engaged in more dialogic reading with fewer technology-related verbalizations and more parent-toddler verbalizations with print books compared with electronic books. Print books elicited a higher quality of parent-toddler collaborative reading experience compared with electronic books.

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Shared book reading is 1 of the most important developmental activities parents can engage in with their children.[1] Shared book reading exposes children to more sophisticated speech and knowledge,[2,3] and provides unhurried time to build attachment,[2,4] in turn promoting executive functioning skills.[5] Nonverbal interactions during shared book reading, such as parental warmth and child enthusiasm, foster interest in reading and are associated with improved literacy later in life.[6,7] In particular, parent dialogic reading practices (comments and questions that go beyond the written word and connect the story to child experiences) are believed to promote child expressive language, engagement, and literacy.[8–10]

With rapid increases in electronic-book and mobile-device ownership,[11,12] a growing amount of children's reading is taking place electronically on electronic readers or tablets. However, pediatricians are unsure whether to promote their use because previous studies suggest both benefits and drawbacks to electronic reading for preschoolers and older children.[13,14] Previous literature has shown that electronic books may facilitate engagement, particularly among reluctant preschoolers and kindergarteners who are learning to read.[14–16] Certain embedded tools, such as dictionaries, may improve vocabulary and story comprehension in kindergarteners.[15,17,18] However, preschoolers and kindergarteners also reproduced fewer narrative details[19] and sequenced story events with lower accuracy after reading enhanced electronic books compared with print books.[13,20] Lower comprehension during electronic-book reading may be due to less adult verbal elaboration[14] and scaffolding[16] and extraneous "hot-spot" enhancements, which may distract from story content.[17] Yet, adult verbal elaboration and parental scaffolding is crucial for young children's learning,[21] particularly regarding digital media.[22–24]

An existing gap in knowledge is how toddlers and parents interact around electronic books. Developmentally, toddlerhood (~24–36 months old) is characterized by emerging language and social-emotional skills as well as immature executive functioning skills. These developmental differences may make toddlers particularly susceptible to the distractions[25] in enhanced electronic books. Additionally, because of their immature memory flexibility, toddlers depend more on adult scaffolding to transfer information from digital media to the real world,[26,27] have more difficulty learning information presented in digital media compared with in-person interactions,[23] and retain information better when digital media are viewed with an adult.[24] Only 1 electronic-book study has been conducted in toddlers, finding that toddlers remembered a novel word better on an electronic book compared with print, but parents read the text and pointed more when interacting over print.[27] This study used an electronic book without digital enhancements that was not commercially available; therefore, results do not generalize to tablet-based books available to families.[22] To our knowledge, no studies have examined dialogic and nonverbal interactions between parents and toddlers when reading electronic books.

For pediatric providers to make informed decisions about recommending electronic books, more needs to be known about differences in parent-child interactions during these types of reading encounters with toddlers, a developmental range that is underrepresented in current literature. In this study, we aim to address these gaps by examining the frequency of parent verbalizations that are important to early language and literacy (eg, dialogic reading), child verbalizations, and quality of the shared book-reading experience during the reading of commercially available electronic and print books.

METHODS

Study Design

We conducted an experimental, laboratory-based study consisting of a video-recorded free play, book-reading protocol, and surveys lasting ~75 minutes. Toddler-parent dyads were assigned to 1 of 36 counterbalanced book-format orders. Parents were compensated $50 for participating. The University of Michigan Institutional Review Board approved this study.

Participants

We recruited 37 parent-toddler dyads from the University of Michigan online research registry (UMhealthresearch.org) and community-based settings, including pediatric offices, child care centers, and community centers. To not bias recruitment toward parents with particular digital media views, language stated generically that the study involved coming to the University of Michigan, where "you and your child would be videotaped while playing with toys and books." Parents contacted researchers via the research registry, e-mail, or phone and underwent phone-based screening. Inclusion criteria were as follows: (1) child age 24 to 36 months, (2) child did not have a developmental delay or serious medical condition, (3) parent read English sufficiently to complete questionnaires and consent, (4) parent was a legal and/or physical custodial guardian, and (5) parent and child did not have uncorrected hearing or vision impairments.

Procedure

At the study visit, parents provided written informed consent. The laboratory room was set up to approximate a living room and contained a 1-way mirror, couches, 3 books in boxes (2 tablet books and 1 print book), and video cameras.

Participants first completed a 5-minute, video-recorded free play with nondigital toys. They then completed a random, preassigned reading activity with an enhanced electronic book, a basic electronic book, and a print book occurring in counterbalanced order (Fig 1). Figure 2 includes 1 example permutation. Books were placed in open boxes labeled 1 to 3 out of children's reach. Parents received instructions to start with the book in box 1, that they have "5 minutes to look at it," and to complete books sequentially as prompted.

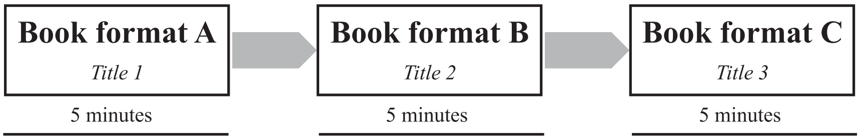

FIGURE 1
Reading protocol. The reading protocol consisted of a preassigned sequential reading activity of an enhanced electronic book, a basic electronic book, and a print book occurring in a counterbalanced fashion in 1 of 6 book-format permutations: (1) enhanced, basic, print; (2) enhanced, print, basic; (3) basic, enhanced, print; (4) basic, print, enhanced; (5) print, basic, enhanced; or (6) print, enhanced, basic. Within each book-format permutation, the order of 3 different book titles was counter-balanced, achieving a total of 36 unique permutations. Thus, all participants read the same 3 books, but not all books were read in the same format or order across participants.

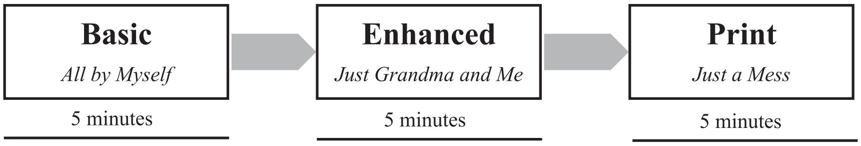

FIGURE 2
Sample of 1 book-reading permutation completed by a participant.

Book Formats

Three Mercer Mayer "Little Critter" books (*Just Grandma and Me, All by Myself*, and *Just a Mess*) were chosen because of their similar length, reading difficulty, and availability in all 3 formats. Print books were 8×8-inch softcovers. Basic electronic-book capabilities allowed for swiping to turn the pages and tapping illustrations to elicit the appearance of words but without autonarration or additional features, such as sound effects. Enhanced electronic books contained audiovisual hot spots: tapping illustrations would result in the appearance and narration of the word (eg, tapping a seagull picture resulted in the appearance and narration of the word "seagull") coupled with sound effects. Tapping other pictures or turning a page produced a sound effect (eg, tapping a dog would produce the sound of a dog panting, and turning the page to a beach produced sounds of ocean waves). Although autonarration of the story was disabled on both electronic-book formats, tapping and holding down an individual sentence in the enhanced electronic book would narrate that text, but this feature was only briefly used by 2 dyads. Basic and enhanced electronic books were preloaded on a 10-inch Samsung Galaxy tablet computer, which contained no other applications. Parents received instruction to select "read it myself" such that the electronic book was not narrating the book text.

Survey Measures

Parents completed surveys regarding covariates for potential inclusion in statistical models, including demographic information (parent age, sex, educational attainment, household income, race and/or ethnicity, relationship to child, and marital status; child's age, sex, ethnicity, and prematurity) and standardized measures of child language, social-emotional development, and digital media–use practices.

The MacArthur-Bates Communicative Developmental Inventory (CDI) short form assessed toddler language development. This 100-word validated[28] and reliable[29] vocabulary checklist generated a percentile score from total words produced and accounted for age.[24]

The Brief Infant-Toddler Social and Emotional Assessment (BITSEA) is a validated[30] and reliable[25] 42-item questionnaire that screens for child social-emotional problems. Parents rated items on a 3-point Likert scale generating the Problem and Competence subscales (Cronbach $\alpha = 0.68$ and 0.58, respectively).

Standardized questions assessed the frequency of home child digital media use (including tablet, smartphone, and electronic-book usage) and parental mediation strategies (instructive, restrictive, and coviewing).[31]

Coding Parent-Toddler Verbal Interactions

We developed a verbal coding scheme based on previous literature on dialogic reading[8] and shared electronic-book reading.[14] For each 10-second interval, researchers coded 1 for a specific verbalization occurring or 0 for not occurring; interval verbalization counts were summed within each 5-minute book condition. Verbalization categories were not mutually exclusive; parents and children could have >1 type per 10-second interval, although each sentence was only coded in 1 category. Please see the coding definitions in Tables 1 and 2 for

TABLE 1 Coding Definitions and Examples of Parent Verbalizations

	Definition	Examples	Cohen's κ
Dialogic	Dialogic reading techniques often prompt a child to expand and elaborate on concepts related to the story. These were defined as follows: parent asks open-ended question, expands on an idea the child has, repeats what the child says, or relates the story content to the child's experience.	"What's happening here?" "What did they do next?" "What did you think about that book?" "Remember when you went to the beach with Dad?" Child says, "Here is a wagon," and parent replies, "a big, red wagon."	0.77
Nondialogic	Nondialogic reading techniques were related to story content but have not been previously shown to elicit the same quantity of child verbalizations as dialogic verbalizations. These were defined as follows: parent labels something, asks a simple question requiring only a name or label, makes a pointing request of the child, makes an attention prompt, or talks about the process of reading.	"What is that?" "Show me the cat." "Look at this!" "There's Grandma!"	0.74
Text read	Parent reads directly from the book text.	"We went to the beach, just grandma and me."	0.86
Format related	These are verbalizations that are related to the book format. Parent comments on, asks a question about, or adds a directive regarding an aspect of the print or tablet interface.	"Great job, you're turning the page!" "Can I hold the book or tablet?" "Go ahead and turn the page." "You can push the button here." "Swipe with your finger."	0.84
Negative format-related directives	Parent makes a negative directive that is related to the book format. For instance, the parent tells the child not to do something related to how the book or tablet functions.	"You can't keep pressing the back button." "Don't turn the page." "Don't rip the book." "Don't turn the volume up." "Don't touch that button."	0.80
Off task	These are unrelated to the book content or book format and include all other parent verbalizations that are not categorized as above.	"You can have your goldfish later." "We are going to the store after this."	0.79

parent and child verbalizations. Parent and child utterances were independently summed to calculate total verbalizations. Undergraduate students blinded to the hypothesis coded to reliability with Cohen's κ of at least 0.70.

Coding Parent-Toddler Nonverbal Interactions

We developed 2 global coding schemes based on existing literature on shared print-book reading to assess parent-toddler nonverbal interactions: shared positive affect[32] and collaborative book-reading experience.[33–35] Codes were applied on the basis of the full 5 minutes per book condition on a scale of 1 to 5 (Table 3). The 5-minute free-play session was also coded for shared positive affect and examined as a potential covariate representing baseline parent-child interaction quality.

Analysis

We conducted Poisson regressions using Proc Genmod to compare each verbal outcome by book format, adjusting for total elapsed time, given the occasional variation in reading duration. Proc Mixed was used to compare differences in positive affect and collaborative book reading by book format. All models included a repeated measures statement to allow for within-subjects comparison of verbal and nonverbal outcomes by book-format condition. Although the counterbalanced design accounted for between-subjects variance in factors known to influence book-reading behaviors, such as sociodemographic characteristics, we included covariates in final models with $P < .05$ to improve model fit (eg, order of book presentation, parent income, race and/or ethnicity, child sex, CDI or BITSEA score, and home media practices). A sensitivity

TABLE 2 Coding Definitions and Examples of Child Verbalizations

	Definition	Examples	Cohen's κ
Book related	Child labels a picture, answers a parent question, repeats what the parent is saying, or talks about a function of the book.	"I want to read this." "I press the button." "Look, a spider!"	0.81
Negative	Child says no or makes a comment in a defiant or negative manner.	"No, Daddy, I do it." "I hold it."	0.71
Other	These are verbalizations that do not fall into the above categories. Unintelligible utterances that are not clearly related to the book were also included.	"Can I have water?" "I want to go home."	0.72

TABLE 3 Nonverbal Coding Definitions

	Shared Positive Affect	Collaborative Book Reading
Definition	Quantity of shared enjoyment between dyad	Quality of shared reading experience
Intraclass correlation	0.84	0.75
Code 1	A score of 1 was marked by little positive shared affect or enjoyment, several instances of negative affect that occur more frequently than instances of positive affect, and/or the child having a tantrum or refusal of prolonged duration or high frequency.	A score of 1 was marked by greater distance between the parent and child, the parent making few attempts to engage the child or being overly directive and/or intrusive, or the child missing social bids from the parent or being confrontational and/or defiant.
Code 3	A score of 3 was marked by small-to-moderate amounts of positive affect between the dyad with brief but unsustained instances of negative affect, or the dyad may be primarily affectively neutral.	A score of 3 was marked by some instances of close dyad proximity with some instances of greater distance between them, some attempts of parent-child engagement but less in frequency than a code 4 or 5, and/or the dyad seeming more focused on the reading task than on each other.
Code 5	A score of 5 was marked by frequent displays of shared positive affect with the dyad showing definite pleasure with each other (eg, high frequency of smiling, laughing, praise, and warmth).	A score of 5 was marked by the dyad being comfortably nestled together with a shared view of the book, a highly responsive parent, and an actively engaged child who exhibits minimal defiance.

analysis excluding 1 participant who cried during the entirety of 1 book-reading condition did not reveal differences; therefore, all participants were included. All analyses were completed in SAS 9.4 (SAS Institute, Inc, Cary, NC).

RESULTS

As shown in Table 4, children were 29.2 months old, and parents were 33.5 years old. Of the parents, 81% were mothers, 76% had a 4-year college degree or more, and 89% were married. Of the children, 54% were boys, 57% were non-Hispanic white, 16% were non-Hispanic African American, and 27% were of other race and/or ethnicity.

Figure 3 shows the number of intervals containing each type of parent verbalization. Parent dialogic verbalizations were greater with print (11.9 intervals [SE = 1.1]) versus either enhanced electronic (6.2 intervals [SE = 0.7]; $P < .001$) or basic electronic books (8.3 intervals [SE = 0.9]; $P < .001$). Parent nondialogic verbalizations were greater with print (17.7 [SE = 0.7]) versus basic electronic books (15.7 [SE = 0.8]; $P = .008$). Parents read the book text more with print (14.3 [SE = 1.0]; $P = .003$) or basic electronic (14.4 [SE = 1.1]; $P < .001$) compared with enhanced electronic books (10.6 [SE = 0.9]). Parents made fewer format-related and negative format-related directives when engaging over print books versus enhanced or basic electronic books (Fig 3). Parents had

TABLE 4 Participant Characteristics (*N* = 37)

Sample	Result
Child age, mo, mean (SD)	29.2 (4.2)
Parent age, y, mean (SD)	33.5 (4.0)
Parent relationship to child, *n* (%)	
Mother	30 (81)
Father	7 (19)
Child sex, *n* (%)	
Boys	20 (54)
Girls	17 (46)
Child race and/or ethnicity, *n* (%)	
White, non-Hispanic	21 (57)
African American, non-Hispanic	6 (16)
Hispanic or other	10 (27)
Parent education, *n* (%)	
Some college courses	4 (11)
2-y college degree	5 (13)
4-y college degree	14 (38)
More than 4-y college degree	14 (38)
Parent marital status, *n* (%)	
Single	4 (11)
Married	33 (89)
Child has used tablet to read a book, *n* (%)	
Almost never	23 (62)
Rarely	2 (5)
Occasionally	4 (11)
Often	6 (16)
Most of the time	2 (5)
Daily time spent reading books together, *n* (%)	
Not used	8 (22)
<30 min	16 (43)
30 min–1 h	9 (24)
1–2 h	3 (8)
3–4 h	1 (3)
CDI percentile, mean (SD)	52.9 (33.4)
BITSEA Problem subscale, mean (SD)	6.7 (3.8)
BITSEA Competence subscale, mean (SD)	19.1 (2.2)

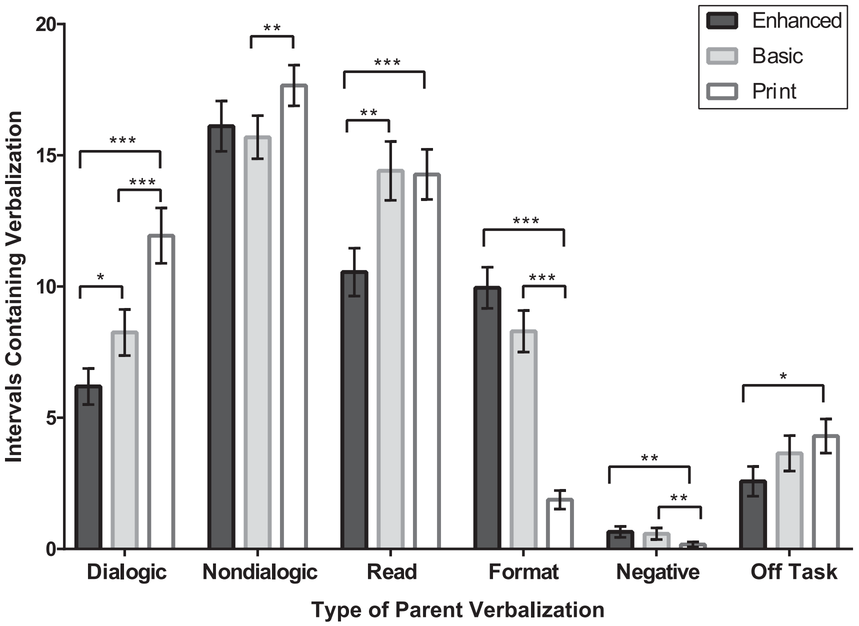

FIGURE 3

Adjusted means for the presence of parent verbalizations occurring with enhanced electronic, basic electronic, and print books. * $P < .05$; ** $P < .01$; *** $P < .001$.

more total verbalizations when interacting over print books (29.5 [SE = 0.2]) versus enhanced electronic books (28.1 [SE = 0.4]; $P = .003$) and more so over basic electronic books (29.3 [SE = 0.3]; $P = .005$) versus enhanced electronic books.

Figure 4 includes the number of intervals containing each type of toddler verbalization. Toddlers' book-content verbalizations were greater with print (15.0 [SE = 1.2]) versus either enhanced electronic (11.5 [SE = 0.9]; $P < .001$) or basic electronic books (12.5 [SE = 1.1]; $P = .005$). Toddlers had no differences in negative verbalizations across all formats but had more off-task verbalizations with print (2.3 [SE = 0.3]) versus enhanced electronic books (1.3 [SE = 0.3]; $P = .007$). Total toddler verbalizations were greater with print (18.8 [SE = 1.1]) versus either enhanced electronic (13.8 [SE = 0.9]; $P < .001$) or basic electronic books (15.3 [SE = 1.0]; $P < .001$).

Figure 5 includes nonverbal outcomes by book format. Shared positive affect was similar across all book formats. Dyads' collaborative book-reading scores were higher with print (3.1 [SE = 0.2]) versus either enhanced electronic (2.7 [SE = 0.2]; $P = .004$) or basic electronic books (2.8 [SE = 0.2]; $P = .02$).

DISCUSSION

Developmental benefits of shared book reading have been attributed to the quality of parent-child interactions occurring around books, particularly in prereaders such as toddlers, who rely heavily on parents to understand story content.[8] These interactions include the quantity of words spoken, how parents tailor content to children's experiences to support learning, and asking open-ended questions to promote child expressive language.[5,8] Our findings suggest that high-quality dialogic practices are less common, and parents and toddlers speak less overall and in a less collaborative manner, when reading electronic books compared with print. Parents read the text less in enhanced electronic books, making more format-related comments and negative directives when reading electronic books.

Similar to previous studies in preschoolers,[17] we found that electronic-book enhancements were likely interfering with parents' ability to engage in dialogic reading. Dialogic, parent-guided conversation promotes toddler expressive-language development and supports preliteracy skills, which are crucial for independent reading,[8] far more than reading only text or making simple (nondialogic) comments, although these are also important.[1] Parents strengthen their children's ability to acquire knowledge by relating new content to their children's lived experiences.[21,36] There is a large body of literature showing that this type of adult scaffolding is especially important for toddlers to transfer information from digital media to the real world because toddlers in particular learn and retain novel information better from in-person interactions than from digital media.[22–24,26,27,37] However, such practices occurred less frequently with electronic books, which raises the question of whether electronic books have lower educational potential for toddlers.

Parents also asked fewer simple questions, commented about the storyline less, and read less during electronic-book conditions compared with print. These behaviors are important because they promote child receptive language by exposing children to novel vocabulary and more complex syntax than conversations occurring during daily activities.[1]

Even interactions over basic electronic books contained fewer dialogic and total parent verbalizations compared with print, suggesting that affordances of the tablet (and not only the interactive design) may be influencing parents' behavior. Parents and children may conceptualize tablets as being

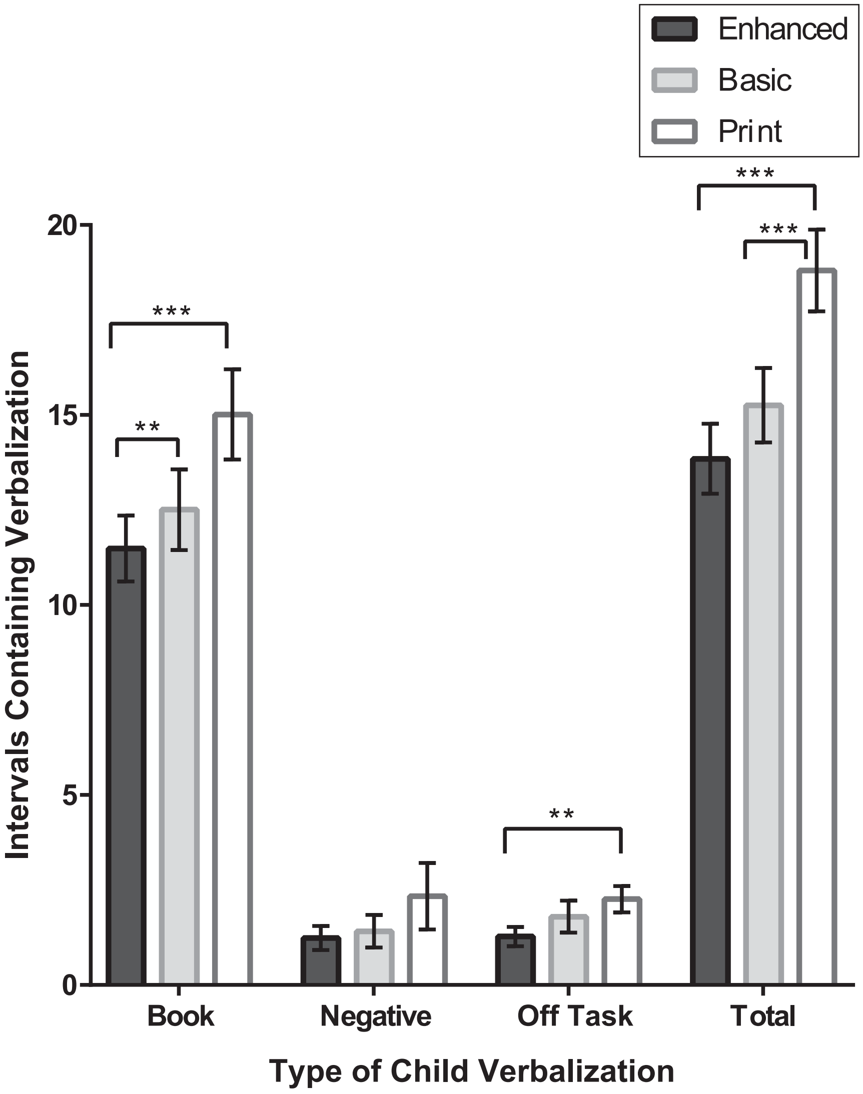

FIGURE 4
Adjusted means for the presence of toddler verbalizations occurring with enhanced electronic, basic electronic, and print books. * $P < .05$; ** $P < .01$; *** $P < .001$.

individually used rather than shared objects. Indeed, 1 study revealed that children tend to create solitary spaces when engaging in tablet play compared with traditional toy play, leaving less space for their parents to coview and ignoring parent bids for attention.[38] Similarly, parents reported a sense of pride and relief when their children independently engaged with a tablet device without help,[39] and we acknowledge that this independence may be perceived as a potential benefit of electronic books. We hypothesize that the tablet itself may reduce opportunities for parent-child interactions during book reading.

Children changed their behavior as a function of book format, verbalizing more when reading the print book. This finding may be related to greater parent dialogic reading with print books versus electronic books, which provides positive reinforcement for toddler speech. Children's tendency to become occupied in repeated tapping or swiping on electronic books may also have supplanted speech production. Repetitive tapping and swiping may not constitute sufficient engagement to learn new concepts because it is thought to represent cause-and-effect play rather than "minds-on" activity.[21] True meaningful engagement (active involvement occurring in a rich social context without distractions) fosters the most effective learning from media.[21] Previous research in preschoolers supports this concept because distracting digital enhancements interfere with parent scaffolding, which leads to reduced child story comprehension and fewer child verbalizations.[13,14] Opportunities to practice expressive language, such as those occurring with print books, are important because early language skills strongly predict future linguistic and cognitive aptitude in school.[40]

The high frequency of format-related verbalizations (eg, directing the child to turn the page) observed during both electronic-book conditions may displace book-related verbal exchanges that dyads engaged in with print books. This is consistent with previous research: although parents showed the same number of verbal exchanges with preschoolers around electronic versus print books, exchanges tended to be related to technology rather than story content.[14] It is possible that parents made more format-related verbalizations to orient their children to a new experience because electronic books were novel to 62% of the children in this sample; however, 79% had previously played with tablets and/or mobile devices. The negative and directive nature of parent format-related verbalizations may indicate a need for more behavioral management with electronic books compared with print.

Parents and children had more off-task verbalizations with the print book versus electronic book, which is similar to previous studies in preschoolers.[14] This could be related to persuasive tablet-design features, which may command parent and

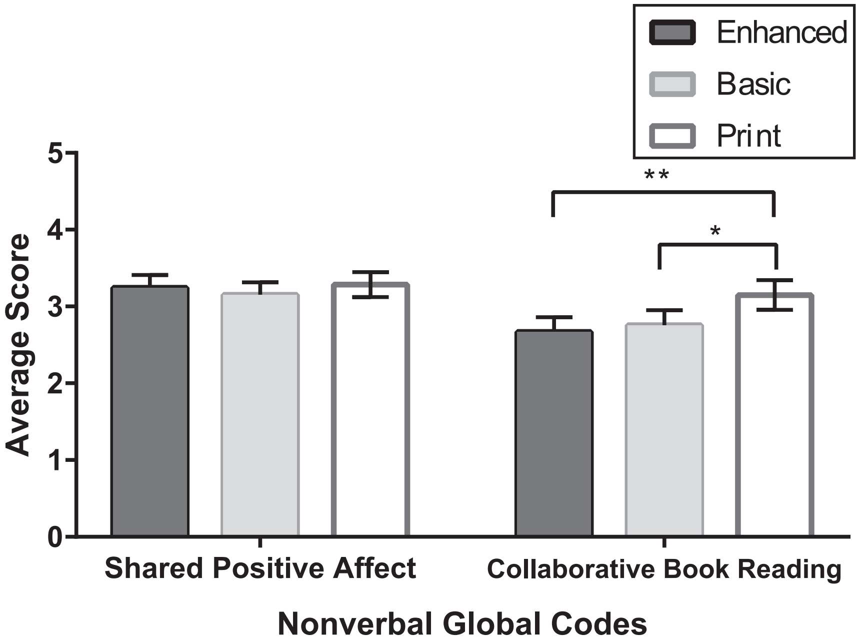

FIGURE 5
Adjusted means (5 = high) for dyad social-emotional outcomes occurring with enhanced electronic, basic electronic, and print books. * $P < .05$; ** $P < .01$.

child attention, at the expense of attending to one another, an effect that is known to occur with traditional screen media, such as television.[41–43] It is challenging to discern whether this attentional focus resulted in improved learning because toddler reading comprehension is difficult to assess. However, as mentioned above, toddlers may be engaged in ways that may be less educationally enriching when reading electronic compared with print books.

Our study was the first to examine nonverbal aspects of electronic-book reading in toddlers both through shared positive affect and collaborative book reading. These nonverbal behaviors during reading are important because they foster a love of reading[7] and promote secure parent-child attachment,[1] which has been implicated in resilience,[44] physical health,[45] and quality of future relationships.[46] Comparable to previous studies in preschoolers,[14] dyads with high shared positive affect consistently showed this across all formats, suggesting that electronic books may be equally enjoyable for dyads despite other limitations. The quality of collaborative reading was likely lower for electronic books because observationally, parents and toddlers frequently sat separately, could not easily view the book, or appeared to struggle for tablet possession. These behaviors during tablet-based play are documented in recent work[38] and merit further study. Our results may explain previous findings that parents report preferring shared reading over print versus electronic books with toddlers.[47]

Limitations include the small sample size from 1 geographic area, the use of only 1 type of book-reading application (which limits generalizability), and that the age range of our study sample precluded assessment of reading comprehension.[48] Strengths include experimental methodology, the use of commercially available books available in 3 formats, a diverse sample, and the within-subjects design, which allowed for direct comparison of the reading experience within each dyad. Future studies should consider other facets of nonverbal interactions or moderating effects of dyad characteristics, such as parent literacy level, child temperament, or home media-use practices. Replication of this study by using different applications (this application had a particular set of enhancements) in other contexts, such as home or school settings, is necessary. Although parent-child interactions are critical for toddler learning, directly examining toddler learning from print versus electronic books is another important area for future work.

CONCLUSIONS

Given the decreased quantity of parent-child verbalizations and quality of interactions occurring with the electronic books that we studied, pediatricians may wish to recommend print books over electronic books with distracting features for parent-toddler shared reading. In considering affordances of electronic books that promote learning, software designers should limit irrelevant audiovisual enhancements for toddlers. Parents reading electronic books with toddlers should consider engaging as they would with print and minimize focus on elements of the technology itself.

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ABBREVIATIONS

BITSEA: Brief Infant-Toddler Social and Emotional Assessment
CDI: Communicative Developmental Inventory

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Differences in Parent-Toddler Interactions With Electronic Versus Print Books

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Infant Deaths in Sitting Devices

Peter Liaw, BS,[a] Rachel Y. Moon, MD,[b] Autumn Han, MD,[c] Jeffrey D. Colvin, MD, JD[d]

abstract

BACKGROUND AND OBJECTIVES: Annually, several hundred infant deaths occur in sitting devices (eg, car safety seats [CSSs] and strollers). Although American Academy of Pediatrics guidelines discourage routine sleeping in sitting devices, little is known about factors associated with deaths in sitting devices. Our objective was to describe factors associated with sleep-related infant deaths in sitting devices.

METHODS: We analyzed 2004–2014 National Center for Fatality Review and Prevention data. The main outcome was sleep location (sitting device versus not). Setting, primary caregiver, supervisor at time of death, bed-sharing, and objects in the environment were compared by using χ^2 tests and multivariable logistic regression. Descriptive statistics of additional possible risk factors were reviewed.

RESULTS: Of 11 779 infant sleep-related deaths, 348 (3.0%) occurred in sitting devices. Of deaths in sitting devices, 62.9% were in CSSs, and in these cases, the CSS was used as directed in $<10\%$. Among all sitting-device deaths, 81.9% had ≥ 1 risk factor, and 54.9% had ≥ 2 risk factors. More than half (51.6%) of deaths in CSSs were at the child's home. Compared with other deaths, deaths in sitting devices had higher odds of occurring under the supervision of a child care provider (adjusted odds ratio 2.8; 95% confidence interval 1.5–5.2) or baby-sitter (adjusted odds ratio 2.0; 95% confidence interval 1.3–3.2) compared with a parent.

CONCLUSIONS: There are higher odds of sleep-related infant death in sitting devices when a child care provider or baby-sitter is the primary supervisor. Using CSSs for sleep in nontraveling contexts may pose a risk to the infant.

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Mr Liaw conducted the initial analyses, interpreted the data, and drafted the initial manuscript; Drs Moon and Han conceptualized and designed the study, interpreted the data, and reviewed and revised the manuscript; Dr Colvin conceptualized and designed the study, performed additional analyses, interpreted the data, and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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WHAT'S KNOWN ON THIS SUBJECT: Each year, a number of infant deaths are associated with sitting devices (eg, car safety seats, strollers, and infant seats). The American Academy of Pediatrics recommends against routine sleeping in sitting devices for infants.

WHAT THIS STUDY ADDS: Using sitting devices for sleeping purposes in nontraveling contexts may pose a risk to the infant.

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Sleep-related infant death is a categorical term that includes sudden infant death syndrome (SIDS), accidental suffocation and strangulation in bed (ASSB), and other ill-defined deaths.[1] Approximately 3700 infants annually suffer sleep-related infant death, making this the leading cause of postneonatal (28 days–1 year old) infant mortality.[2]

In an effort to decrease the rate of sleep-related deaths, the American Academy of Pediatrics (AAP) has released recommendations for a safe infant sleep environment.[1] Those recommendations include placing the infant in a supine sleep position, using a firm sleep surface, room-sharing without bed-sharing, avoiding the use of soft bedding and overheating, and particularly regarding sitting devices, refraining from the use of sitting devices, such as car safety seats (CSSs) and strollers for routine sleep.[1]

Sitting and carrying devices (such as CSSs, strollers, infant seats, bouncers, and swings) were initially designed primarily for the transporting, feeding, and play of infants and young children. Despite the intended purpose of these devices (eg, transportation, feeding, and playing), infants spend a significant amount of time in sitting devices for other reasons. One observational study of 187 infants found that the mean time an infant spent in a sitting device was 5.7 hours (range 0–16 hours) per day.[3] In some cases, these devices are used as a sleep alternative to a crib or bassinet.[3–6]

When placed in a sitting device for a reason other than its intended purpose (ie, not being used for transportation, feeding, or playing), infants are at risk for injury, including falls from the devices, falls from elevated surfaces on which the device has been placed, and injuries when the device flips over on a soft surface.[7–10] Additionally, in 1 retrospective study of sleep-related deaths of young (<2 years old) children occurring in sitting devices, many parents used the device as a place for their children to sleep; 16 of the 18 deaths involving a CSS occurred outside a motor vehicle, suggesting use of the CSS other than for its intended purpose.[5] Similarly, a UK study of 14 CSS-related infant deaths between 1999 and 2011 found that most deaths occurred when the CSSs were not being used to transport an infant in a motor vehicle and that most of these deaths occurred in infants <2 months of age.[4]

Reports of infant deaths in sitting devices have thus far included a limited number of deaths and primarily focused on the intended use of the sitting device at the time of death. Little is known about other factors surrounding infant deaths in sitting devices. In this study, we analyzed data from a large US case-reporting system to better understand the factors associated with sleep-related infant deaths in sitting devices.

METHODS

Data Source

Data for this study were obtained from the National Center for Fatality Review and Prevention (NCFRP). The NCFRP, funded by the Maternal and Child Health Bureau, Health Resources and Service Administration, US Department of Health and Human Services (UG7MC28482), and US Centers for Disease Control and Prevention, is a Web-based system used for systematically collecting, analyzing, and reporting data on infant and child deaths.[11] After approval and consent from the 45 states participating in the NCFRP, we received a deidentified data set of infant deaths occurring during sleep or in a sleep environment from 2004 to 2014. The NCFRP Child Death Review Case Reporting System has been previously described.[11–13]

Study Subjects

The NCFRP provided data on all infant (≤365 days of age) deaths occurring during sleep. Deaths that could be explained by nonsleep-related causes, such as homicide or infection, and deaths missing sleep location were excluded. By using data regarding cause-of-death determination, cases were assigned to 1 of 3 causes of death: SIDS or sudden unexpected infant death (SUID), ASSB, and unknown or undetermined.

Sleep Location and Setting of Death

We categorized sleep location as the location in which the infant death occurred; deaths were dichotomized into those in sitting devices (CSSs, strollers, bouncers, swings, and other infant seats) or not in sitting devices (crib, bassinet, playpen, adult bed, and couch or chair). Infant slings and carriers and nursing pillows were not categorized as sitting devices. Setting of death was defined as the environment in which the infant death occurred and was categorized as follows: child's home; relative's or friend's home; foster home; child care center or baby-sitter's home; vehicle in motion or temporarily stopped or parked; shopping or errands or car seat or stroller on a walk; motel, recreational vehicle or trailer, or park; and other.

Primary Caregiver and Primary Supervisor

The primary caregiver was defined as the person who was responsible for the infant on a daily basis and was categorized as a parent or guardian, foster parent, relative or friend, or other. Primary supervisor was defined as the person who was responsible for the infant at the time of death and was categorized as a parent or guardian, relative, friend, child care provider (licensed or unlicensed), baby-sitter, other, or unknown.

Data Analysis

Data analysis was performed by using SAS (SAS Institute, Inc, Cary, NC) and SPSS (IBM SPSS Statistics, IBM Corporation, Armonk, NY). As previously described,[12,13] multiple imputations using the Markov chain Monte Carlo method were performed to impute missing data, and subsequent analyses were performed by using pooled imputed data. The maximum missing data that were imputed for any variable was 2.2% (setting and race and/or ethnicity). $P < .05$ was considered significant. First, any available narratives and free-text variables were reviewed to determine if the sitting device was being used as directed at the time of death. CSS use guidelines stipulate that they be used for transport in a vehicle (either parked or in motion).[14] However, CSSs are now being marketed to also be used for transport other than in a vehicle (eg, stroller and shopping cart). Hazard patterns noted in case series of injuries and deaths associated with CSSs[5,8] suggest that many injuries and deaths are associated with improper buckling of CSS straps. Thus, we defined "as directed" use of a CSS as the infant being strapped into an appropriately sized CSS while the infant was being transported in a vehicle (either parked or in motion.) For deaths in sitting devices, we determined the number of risk factors present at the time of death[15] and categorized them as follows: (1) infant risk factors (estimated gestation age <37 weeks; birth weight <2500 g; intrauterine exposure to illicit drugs, heavy alcohol use, or misuse of over-the-counter medications; infant disability or chronic health condition; and maternal pregnancy complications), (2) supervision risk factors (supervisor impaired because of alcohol or illicit drugs, supervisor with a history of drug or alcohol abuse, or supervisor absent, asleep, or distracted), and (3) sleep-environment risk factors (new sleep environment, item in the sleep environment, or exposure to secondhand smoke). Bed-sharing and sleep position were not included as risk factors given their relative rarity in or irrelevance to deaths occurring in sitting devices. Narratives available for deaths in CSSs (*n* = 24) were also examined to identify hazards not included as variables in the data set. Those hazards were described separately for deaths in which the CSS was and was not used as directed. Second, using the χ^2 test, we compared risk factors by sleep location (in a sitting device versus not in a sitting device) and by whether the CSS was used as directed. Multivariable logistic regression, adjusting for age, race and/or ethnicity, and sex, was used to calculate the adjusted odds ratios (aORs) of the cause of death, primary supervisor, bed-sharing, and any objects being present in the sleep environment.

RESULTS

Characteristics of Deaths in Sitting Devices

Of 11 779 sleep-related infant deaths that were included in the analysis, 348 (3.0%) occurred in sitting devices (Table 1). The majority of deaths in sitting devices occurred in CSSs (219; 62.9%), followed by bouncers, swings, and other (122; 35.1%) and strollers (7; 2.0%). The median age of infants dying in sitting devices was 2.0 months (interquartile range 1.0–4.0 months). The sitting device was not used as directed in nearly two-thirds of deaths (62.9%). Among the 219 deaths in CSSs, <10% (*n* = 20) occurred in the context of the CSS being used as directed (ie, the infant being strapped into an appropriately sized CSS while the infant was being transported in a vehicle, either parked or in motion) or when it was unclear if the CSS was being used as directed. Among all deaths in any sitting device, more than three-quarters (81.9%) had a least 1 risk factor, and more than half (54.9%) had 2 or more risk factors. Among deaths in any sitting device in which the device was used as directed or when it was unclear whether it was being used as directed (*n* = 131), the most common risk factors were the supervisor being asleep (*n* = 44; 33.6%), maternal pregnancy complications (*n* = 32; 24.4%), infant exposure to secondhand smoke (*n* = 30; 22.9%), and having an estimated gestational age <37 weeks (*n* = 30; 22.9%). Other risk factors that were present in >15% of deaths in which the sitting device was being used as directed or when it was unclear whether it was being used as directed include the following: item present in the sleep environment (*n* = 26; 19.8%), new sleep environment (*n* = 23; 17.6%); and low birth weight (*n* = 21; 16.0%). A risk factor was present in approximately half of each of the 3 domains: infant risk factors (46.6%), supervision risk factors (48.9%), and sleep-environment risk factor (48.1%). Half of the deaths (50.4%) had risk factors in at least 2 of the 3 domains.

We also examined risk factors associated with the subset of deaths occurring in CSSs when they were used as directed and compared those to risk factors in deaths when the CSS was not used as directed. Although the comparison was likely underpowered, the only significant difference was for a supervisor being asleep at the time of death (CSS used as directed 6.3% versus CSS not used as directed 32.0%; $P = .044$; Appendix Table). This association was no longer significant in logistic regressions adjusted for age and sex.

Among deaths in CSSs, additional information was available from narratives (of variable length) for 24 of the deaths, 7 of which occurred when the CSS was used as directed and 17 occurred when the CSS was not used as directed. Among deaths in which the CSS was used as directed, the entire CSS was covered with a blanket in 2 deaths; 1 infant was loosely buckled or not fully buckled into the CSS and was overheated, and 1 infant was left alone in a car in the CSS for a prolonged period of time. In

TABLE 1 Characteristics of the Study Population by Location of Death

Characteristics	Total (*N* = 11 779), *n* (%)	Not a Sitting Device (*n* = 11 431), *n* (%)	Sitting Device (*n* = 348), *n* (%)	*P*
Age at the time of death, mo				
0–3	8190 (69.3)	7951 (69.6)	239 (68.7)	.29
4–6	2638 (22.4)	2551 (22.3)	87 (25.0)	
7–11	951 (8.1)	929 (8.1)	22 (6.3)	
Infant sex				
Male	6823 (57.9)	6623 (57.9)	200 (57.5)	.84
Female	4956 (42.1)	4808 (42.1)	148 (42.5)	
Race and/or ethnicity of infant				
Hispanic	2032 (17.3)	1968 (17.2)	64 (18.4)	.63
Non-Hispanic white	5272 (44.8)	5112 (44.7)	160 (46.0)	
Non-Hispanic African American	3733 (31.7)	3626 (31.7)	107 (30.8)	
Other	742 (6.3)	725 (6.3)	17 (4.9)	
Cause of death				
SUID or SIDS	3278 (27.8)	3151 (27.6)	127 (36.5)	<.0001
ASSB	3407 (28.9)	3349 (29.3)	58 (16.7)	
Unknown or undetermined	5094 (43.3)	4931 (43.1)	163 (46.8)	
Primary caregiver at time of death				
Parent or guardian	11 458 (97.3)	11 118 (97.3)	340 (97.7)	.80
Relative or friend	182 (1.6)	179 (1.6)	[a]	
Foster parent	102 (0.9)	99 (0.9)	[a]	
Other	37 (0.3)	35 (0.3)	[a]	
Primary supervisor at time of death				
Parent or guardian	9004 (76.5)	8743 (76.5)	261 (75.0)	.0007
Relative	662 (5.6)	649 (5.7)	13 (3.7)	
Friend	85 (0.7)	82 (0.7)	[a]	
Baby-sitter	398 (3.4)	375 (3.3)	23 (6.6)	
Child care provider	157 (1.3)	145 (1.3)	12 (3.5)	
Other	45 (0.4)	44 (0.4)	[a]	
Unknown	1425 (12.1)	1390 (12.2)	35 (10.1)	
Setting				
Child's home	9444 (80.2)	9221 (80.7)	223 (64.1)	<.0001
Relative's or friend's home	1423 (12.1)	1365 (11.9)	58 (16.7)	
Foster home	123 (1.0)	121 (1.1)	[a]	
Child care center or baby-sitter's home	511 (4.3)	480 (4.2)	31 (8.9)	
Motel, RV, trailer, or park	112 (1.0)	103 (0.9)	9 (2.6)	
Vehicle in motion or temporarily parked	20 (0.2)	[a]	19 (5.5)	
Shopping or errands (not in vehicle), restaurant, or on walk in stroller	8 (0.1)	[a]	[a]	
Other	138 (1.2)	136 (1.2)	[a]	
Bed-sharing				<.0001
Yes	6604 (56.1)	6589 (57.6)	15 (4.3)	
No	5175 (43.9)	4842 (42.4)	333 (95.7)	
≥1 object in sleep environment				<.0001
Yes	3954 (33.6)	3883 (34.0)	71 (20.4)	
No	7825 (66.4)	7548 (66.0)	277 (79.6)	

RV, recreational vehicle.

[a] Frequency suppressed because cell size <6.

the 3 other deaths in which the CSS was used as directed, there were no obvious hazards noted, although 1 infant had a history of extreme prematurity (<28 weeks estimated gestational age) and extremely low birth weight (<1000 g). Among the deaths in which the CSS was not used as directed, 4 deaths occurred when the infant was loosely buckled or not fully buckled into the CSS, 2 occurred while the entire CSS was covered by a blanket, and in 1 death, the CSS had shifted position in a dangerous manner. In 8 deaths in which the CSS was not used as directed, there were no obvious hazards, although in all but 3 of these deaths, the infant had a risk factor present: supervisor asleep (*n* = 3); intrauterine exposure to illicit drugs, heavy alcohol use, or misuse of over-the-counter medications (*n* = 2); prematurity (*n* = 1); and an item present in the sleep environment (*n* = 1).

Comparison of Deaths in Sitting Devices to Deaths Not in Sitting Devices

A higher proportion of infants who died in sitting devices had SUID or SIDS or an unknown or undetermined cause of death compared with infants who did not die in sitting devices ($P < .0001$; Table 1). The majority of deaths occurring both in sitting devices and not in sitting devices occurred in the child's home. Nearly two-thirds (64.1%) of deaths in sitting devices, including 74.3% of deaths in strollers and more than half (51.6%) of deaths in car seats, occurred in the child's home. Among deaths in sitting devices, higher percentages of deaths in CSSs occurred at a relative's or friend's home (21.9%) and at a child care center or baby-sitter's home (12.3%) than deaths in strollers and bouncers or swings (total percentage at both locations 11.5%; $P < .0001$).

After adjusting for age, sex, and race and/or ethnicity and in comparison with deaths that did not occur in a sitting device, deaths in sitting devices had higher odds of occurring under nonparental supervision, such as baby-sitters (aOR 2.0; 95% confidence interval [CI] 1.3–3.2) and child care providers (aOR 2.8; 95% CI 1.5–5.2), than deaths occurring under parental supervision (Table 2). Relative to infants who died while not in sitting devices, infants who died in a sitting device were half as likely to have an object in the sleep environment (aOR 0.5; 95% CI 0.4–0.6) or to have a cause of death of ASSB (aOR 0.4; 95% CI 0.3–0.6; reference = SIDS and SUID).

TABLE 2 Multivariable Analysis of Risk Factors of Infant Deaths in Sitting Devices Compared With Deaths Not Occurring in a Sitting Device

Characteristics	Odds Ratio (95% CI)[a]	*P*
Primary supervisor at the time of death		
Relative	0.7 (0.4–1.2)	.16
Friend	1.1 (0.4–3.7)	.83
Baby-sitter	2.0 (1.3–3.2)	.002
Child care provider	2.8 (1.5–5.2)	.002
Other	0.7 (0.1–5.2)	.75
Unknown	0.8 (0.6–1.2)	.35
Parent or guardian	Reference	—
Cause of death		
ASSB	0.4 (0.3–0.6)	<.001
Unknown or undetermined	0.8 (0.7–1.1)	.14
SUID or SIDS	Reference	—
Bed-sharing		
Bed-sharing	0.03 (0.02–0.05)	<.001
Not bed-sharing	Reference	—
≥1 object in sleep environment		
Item present	0.5 (0.4–0.6)	<.001
No item present	Reference	—

—, not applicable.

[a] Adjusted by age category, sex, and race and/or ethnicity. Reference is death not occurring in a sitting device.

DISCUSSION

In this large data set of 11 779 infant sleep-related deaths, 3% occurred in a sitting device, consistent with other published data.[6,16] The majority of deaths in sitting devices were in CSSs. The overwhelming majority of infants who died in sitting devices died at home and under the supervision of their parent or guardian. Because there are no data available on the relative amount of time infants spend sleeping in cribs, bassinets, sitting devices, and other locations, this study cannot compare the relative risk of sleeping in a sitting device compared with other locations. However, these results do serve as a reminder that sleep-related infant deaths do occur in sitting devices, including CSSs.

CSSs are a safe and effective way of transporting an infant and should always be used when transporting an infant in a motor vehicle, whether the infant is awake or asleep. The AAP notes that CSSs are designed as safety devices to be used in motor vehicles and not as general infant sitting devices[14] and advises that they be used only for travel.[14,17] If a child falls asleep in a CSS while actively traveling in a motor vehicle, they should remain in the CSS until they are no longer traveling. If they are still asleep when they are no longer traveling, they should then be placed in a crib or bassinet. Thus, theoretically, few deaths in sitting devices should occur outside of traveling contexts. However, our findings indicate that in the great majority of deaths in sitting devices, the infant was not being transported. Although parents and other caregivers may put an infant in a sitting device with the intent of sleep, the AAP recommends against this because of safety concerns. Although we cannot ascertain from this study all of the circumstances surrounding the infant at the time of death, we believe that it is prudent for parents and caregivers to remove the infant from the sitting device when they fall asleep and place them in a bassinet or crib when they are not transporting the infant in a motor vehicle. After leaving the motor vehicle, infants should be moved to a flat, firm surface when it is practical to do so.[1] At a minimum, infants should not sleep in these devices unsupervised. Although this data set did not provide detail regarding buckling, a previous study found that several infants who died in sitting devices had not being properly buckled,[5] and we agree that infants should also always be buckled with a 5-strap harness, even when asleep, to reduce the risk of strangulation and positional asphyxia. Pediatricians should encourage parents and caregivers to include a portable crib or bassinet when traveling for use once they reach their destination if it is likely that their infant will be asleep.

Despite AAP recommendations, infants often spend prolonged periods of time in CSSs when not traveling, and the CSS frequently is used as an alternative to a crib or bassinet.[3–6] This may in part be because CSSs are ubiquitous and because they are convenient for parents and caregivers to use. Indeed, our analysis revealed that nearly two-thirds of deaths in sitting devices occurred in the context of a sitting device that was not being used as directed or for its intended purpose. This is consistent with US Consumer Product Safety Commission injury data that estimate that >8000 infants are evaluated each year in hospital emergency departments for injuries associated with CSSs that are sustained outside of a motor vehicle.[8]

It is likely that caregivers find CSSs and other sitting devices to be a convenient means of temporarily holding a child while the caregiver is busy with other tasks. Caregiver confidence in the safety of CSS also is likely an important driver of the behavior. Knowing that CSSs are for safety and are "approved," some caregivers may also believe that the use of CSSs for purposes outside of travel are also safe. Additionally, financial constraints may play a role in the inappropriate use or overuse of sitting devices for sleeping purposes. Although this study did not look at the motive behind placing an infant in a CSS for nontransportation reasons, it is worth considering that some caregivers might have been unable to afford a portable crib or other flat sleeping surface and used a CSS instead.

Although the majority of deaths in sitting devices were at home and under the supervision of a parent or guardian, when compared with other deaths, infants dying in sitting devices had higher odds of having a child care provider or baby-sitter as the primary supervisor at the time of death (compared with a parent or guardian). Nonparental caregivers should be advised not to keep infants in sitting devices for sleep. Additionally, environments such as a relative's or friend's home may not be well equipped to safely accommodate the infant during sleep. In such cases, the use of a portable crib or bassinet should be arranged. Recent campaigns to educate child care providers on safe sleep-environment practices have been successful in improving knowledge and safe sleep practices.[18] However, these findings suggest that there are still gaps in the public knowledge regarding the appropriate usage of sitting devices for infant care and that all caregivers, including nonparental caregivers, must be educated in this regard.

This study has several limitations. Despite the NCFRP being a large case-reporting system, not every state participates, and only infant deaths reviewed by infant and child fatality teams are generally reported. Therefore, the NCFRP may not include all infant deaths in the participating states. Without denominator data, it is not possible to compare the collected data with vital statistics. As a result, it is not possible to determine the relative risk of infant sleep in a sitting device compared with a crib or bassinet. Additionally, some data items were collected from caregiver interviews, and thus, recall bias and missing data are limitations. Furthermore, the quality of data is dependent on the reporter's experience and personal interpretation, and there may have been variability in how data were reported. In our examination of deaths in sitting devices, it is possible that some supervisors whom we deemed as being impaired because of distraction, illness, or disability were still capable of supervising the infant; however, these deaths comprised a small minority of the deaths in sitting devices. In addition, not all risk factors included in our analysis of deaths in sitting devices (eg, maternal pregnancy complications) have been definitely linked to a heightened risk of infant sleep-related mortality. Finally, the absence of narratives and character limits on the narratives and other free-text variables posed another challenge in fully understanding the context in which an infant died in a sitting device.

CONCLUSIONS

Deaths in sitting devices comprise ~3% of all infant sleep-related deaths, with the majority of these deaths occurring in CSSs. The majority of sitting-device–related infant deaths occur in nontraveling situations. Although our study does not examine why these factors are associated with infant death in sitting devices, our findings underline the significance of educating caregivers about the importance of using sitting devices only for their intended purpose, such as using CSSs only for transportation. Sitting devices are not an acceptable substitute for a crib or bassinet. Using CSSs for sleep in nontraveling contexts may pose a risk to the infant.

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ABBREVIATIONS

AAP: American Academy of Pediatrics
aOR: adjusted odds ratio
ASSB: accidental suffocation or strangulation in bed
CI: confidence interval
CSS: car safety seat
NCFRP: National Center for Fatality Review and Prevention
SIDS: sudden infant death syndrome
SUID: sudden unexpected infant death

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POTENTIAL CONFLICT OF INTEREST: In 2016, Dr Moon testified as a paid expert witness in a case of sleep-related infant death; Mr Liaw and Drs Han and Colvin have indicated they have no potential conflicts of interest to disclose.

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Antibiotic Prescribing During Pediatric Direct-to-Consumer Telemedicine Visits

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abstract

BACKGROUND AND OBJECTIVES: Use of commercial direct-to-consumer (DTC) telemedicine outside of the pediatric medical home is increasing among children, and acute respiratory infections (ARIs) are the most commonly diagnosed condition at DTC telemedicine visits. Our objective was to compare the quality of antibiotic prescribing for ARIs among children across 3 settings: DTC telemedicine, urgent care, and the primary care provider (PCP) office.

METHODS: In a retrospective cohort study using 2015–2016 claims data from a large national commercial health plan, we identified ARI visits by children (0–17 years old), excluding visits with comorbidities that could affect antibiotic decisions. Visits were matched on age, sex, chronic medical complexity, state, rurality, health plan type, and ARI diagnosis category. Within the matched sample, we compared the percentage of ARI visits with any antibiotic prescribing and the percentage of ARI visits with guideline-concordant antibiotic management.

RESULTS: There were 4604 DTC telemedicine, 38 408 urgent care, and 485 201 PCP visits for ARIs in the matched sample. Antibiotic prescribing was higher for DTC telemedicine visits than for other settings (52% of DTC telemedicine visits versus 42% urgent care and 31% PCP visits; $P < .001$ for both comparisons). Guideline-concordant antibiotic management was lower at DTC telemedicine visits than at other settings (59% of DTC telemedicine visits versus 67% urgent care and 78% PCP visits; $P < .001$ for both comparisons).

CONCLUSIONS: At DTC telemedicine visits, children with ARIs were more likely to receive antibiotics and less likely to receive guideline-concordant antibiotic management compared to children at PCP visits and urgent care visits.

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Dr Ray designed the study, supervised analysis, interpreted the data, and drafted the manuscript; Ms Shi conducted the analyses and interpreted the data; Dr Poon assisted with analysis and interpreted the data; Drs Gidengil and Uscher-Pines assisted with the study design and interpreted the data; Dr Mehrotra designed the study, acquired the data, supervised analysis, and interpreted the data; and all authors critically revised the manuscript, approved the final manuscript as submitted, and agree to be accountable for the work.

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WHAT'S KNOWN ON THIS SUBJECT: Authors of previous studies identified concerns about antibiotic prescribing for adults using direct-to-consumer (DTC) telemedicine. No study has examined antibiotic prescribing during pediatric DTC telemedicine visits.

WHAT THIS STUDY ADDS: Compared with urgent care and primary care visits, children receiving care for acute respiratory infections during DTC telemedicine visits are more likely to receive antibiotics and less likely to receive guideline-concordant antibiotic management.

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Many commercial companies offer direct-to-consumer (DTC) telemedicine visits in which patients are connected to physicians outside of the medical home through audio-only or audio-video conferencing on their personal devices.[1] DTC telemedicine companies highlight the convenience of this care and report high patient satisfaction.[2–4] Access to telemedicine has expanded, with 96% of large business insurance plans now offering coverage for employees and their families.[5] As a result, millions of children now have access to DTC telemedicine, and use is rapidly increasing.[6]

The American Academy of Pediatrics discourages the use of DTC telemedicine outside of the medical home for acute pediatric care, citing concerns such as limited physical examination capabilities, lack of ongoing patient-provider relationships, and lack of access to patient records, all of which may lead to lower-quality care.[7] The American Academy of Pediatrics further notes that these issues may be particularly important with children who may have difficulty verbalizing their symptoms.[7] The American Telemedicine Association echoed many of these concerns,[8] adding that the use of personal devices may also impact technical quality and privacy of care. The American Telemedicine Association further suggests that DTC telemedicine outside of the medical home should not be used for children <2 years old.[8] Both organizations emphasize the need for telemedicine visits to adhere to the same standards expected of in-person care, including adherence to professional guidelines for appropriate examination, diagnostic testing, and treatment.[7,8]

To date, there is limited evidence regarding the quality of care during pediatric DTC telemedicine visits. Early studies of adult patients using DTC telemedicine compared with physician office visits have identified more inappropriate antibiotic prescriptions for bronchitis[9] and more broad-spectrum antibiotic use.[10] The quality of DTC telemedicine care for children may differ for several reasons. First, there is heightened reliance on the physical examination among children who cannot fully articulate symptoms.[7] Second, care requires knowledge of pediatric-specific guidelines.[11–13] Third, rates of guideline-concordant antibiotic management at physician visits is higher for children than for adults[14]; therefore, the relative difference in quality of care at DTC telemedicine visits may be different.

To fill this gap in knowledge about the quality of commercial DTC telemedicine care for children, we used data from a large national health plan to compare the quality of antibiotic prescribing for acute respiratory infections (ARIs) at pediatric DTC telemedicine, urgent care, and primary care provider (PCP) visits. We focus on ARIs because authors of previous studies identified concerns about antibiotic prescribing during pediatric ARI visits in other settings,[14–19] and because ARIs account for the majority of DTC telemedicine visits.[6]

METHODS

Study Population

We performed a retrospective cohort study using 2015–2016 claims data from a large national commercial health plan, which provides coverage for roughly 4 million children annually from all 9 census divisions and contracts with a single national DTC telemedicine vendor. Children age 0 to 17 years were included, with no minimum enrollment duration requirement. We excluded children who lacked pharmaceutical coverage during the month of their visit to ensure record of pharmacy claims.

Identifying ARI Visits

ARI visits were identified by using previously published methods on the basis of *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) codes.[15,20,21] Consistent with previous work,[14,15,20,21] ARI diagnoses included diagnoses for which antibiotics may be warranted (sinusitis [461.x], pneumonia [481.x–483.x, 485.x–486.x], streptococcal pharyngitis [034.x], acute otitis media [382.x]) and diagnoses for which antibiotics are not warranted (eg, viral upper respiratory infection [URI], bronchiolitis, viral pharyngitis, serous otitis media [381.x, 460.x, 462–466.x, 480.x, 490.x]). We excluded bacterial pneumonia visits because of the small number of DTC telemedicine visits identified (n = 11). We converted *International Classification of Diseases, 10th Revision, Clinical Modification* (ICD-10-CM) codes to ICD-9-CM codes using a modified crosswalk created by the Centers for Medicare and Medicaid Services (see Supplemental Table 5).[22]

To examine the first ARI visit within an episode of illness, we identified "index" ARI visits with no ARI visits at any location in the previous 21 days, which is consistent with previous studies.[10,23] Subsequent ARI visits within 21 days of an index visit were considered follow-up care. We excluded episodes as detailed in Supplemental Fig 2. Using a previously published methodology, we excluded episodes for which the index visit included a diagnosis indicating chronic conditions (eg, history of transplant) or additional codiagnoses (eg, urinary tract infection) that could impact antibiotic prescribing decisions (n = 60 947; 4.7%) (Supplemental Table 6).[15,21] These exclusion criteria were originally developed for adult populations. Although not all of these exclusion criteria are reasons to deviate from pediatric ARI guidelines, we applied them to study a set of visits consistent with other studies.

Identifying Setting of Care

ARI episodes were categorized as DTC telemedicine, urgent care, or PCP on the basis of the index visit setting. We identified setting using place of service codes, Current Procedural Terminology codes, insurer provider specialty codes, and organizational national provider identifiers and tax identification numbers for urgent care and DTC telemedicine companies through previously described methods (additional details in Supplemental Information).[24] ARI episodes that began with index visits to settings other than DTC telemedicine, urgent care, or PCP offices (eg, emergency department, retail-based clinics) were not included.

Outcomes

Our 2 primary outcomes, compared across settings, were (1) the proportion of visits that resulted in an antibiotic prescription and (2) the proportion of visits that resulted in antibiotic management that was concordant with guidelines for the visit diagnosis.

We identified all filled prescriptions on the day of the index visit and subsequent 2 days and assigned these to the index visit, consistent with previous methods.[1,10,25] We included all systemic antibiotics (ie, oral, intramuscular) and excluded topical, ophthalmic, or otic antibiotics. We determined guideline concordance of antibiotics with visit diagnosis, assigning each visit to 1 of 5 categories (Supplemental Table 7).[21,26] "Antibiotic prescribed" visits included visits categorized as guideline-concordant antibiotic use, guideline–non-concordant antibiotic use, and unnecessary antibiotic use. "Guideline-concordant antibiotic management" included visits categorized as guideline-concordant antibiotic use for sinusitis, otitis media, or streptococcal pharyngitis (ie, amoxicillin or amoxicillin-clavulanic acid for sinusitis,[12] amoxicillin or amoxicillin-clavulanic acid for otitis media,[11] and penicillin or amoxicillin for streptococcal pharyngitis[27]), no antibiotic use for sinusitis or otitis media (also guideline-concordant management for these diagnoses[11,12]), or guideline-concordant nonuse of antibiotics for diagnoses that do not warrant antibiotics (eg, bronchiolitis[13]).

As secondary outcomes, we compared the occurrence of streptococcal testing within 1 day for children diagnosed with streptococcal pharyngitis[27] as well as return visits within 2 and 21 days of an index visit to any setting (eg, PCP, DTC telemedicine, urgent care, retail clinic, emergency department). We did not have streptococcal testing results.

Patient and Visit Characteristics

Patient age, sex, and high-deductible health plan (HDHP) status were determined from insurance enrollment files. Using the patients' zip code, we determined census region and rural-urban commuting area codes.[28] We determined patient chronic medical complexity using the Pediatric Medical Complexity Algorithm Version 2 applied to 2014–2016 inpatient and outpatient claims.[29] This algorithm is used to identify children with 3 levels of chronic medical complexity: complex chronic disease, noncomplex chronic disease, and no chronic disease.[29]

Matching

To address differences in patients and conditions managed in the 3 settings, we used coarsened-exact matching,[30] which prunes observations to achieve covariate balance between groups. Instead of matching to a fixed number of visits, coarsened-exact matching matches DTC telemedicine visits to many matched urgent care visits and PCP visits and then weights each stratum or matched set.[30] Specifically, we matched DTC telemedicine visits to urgent care visits and separately to PCP visits on the basis of age (in years), sex, chronic medical complexity, state, rural or urban area, HDHP status, and diagnosis category (eg, otitis media, viral URI).

Statistical Analysis

Across ARI visits for the 3 settings of care, we described patient characteristics and diagnoses. In the unmatched sample and the matched weighted sample, we examined antibiotic prescribing and guideline-concordant antibiotic management for DTC telemedicine visits compared with urgent care and compared with PCP offices using χ^2 tests. We include both unmatched and matched results because of potential subjectivity in diagnoses, which may then drive variability in antibiotic prescribing.[16] In the matched weighted sample, we also compared streptococcal testing and return visits by setting using χ^2 tests. We adjusted for multiple comparisons in our main results using the Benjamini-Hochberg false discovery rate,[31] yielding a *P* value of .0342.

To examine whether differences in antibiotic prescribing varied by patient characteristics, we performed further analysis that was focused on 2 variables that may impact guideline adherence: child age and chronic medical conditions. Within each category of child age and medical complexity, we examined antibiotic testing and guideline concordance for DTC telemedicine compared with urgent care and PCP offices using χ^2 tests and then tested the significance of an interaction term between age or medical complexity and visit setting using logistic regression.

We performed 2 sensitivity analyses to examine the robustness of our findings to specific assumptions. First, we conducted a sensitivity analysis in which we redefined guideline-concordant antibiotic management so that it no longer included "no antibiotic use" for sinusitis and otitis. Because guidelines allow for observation without antibiotic use in specific circumstances for sinusitis and otitis media.[11,12] we considered no antibiotic use to be a guideline-concordant management option for these diagnoses in our main analysis but not in this sensitivity analysis. Second, we examined antibiotic prescribing and guideline-concordant management after excluding ARI visits with a follow-up visit within 2 days because visits with such early follow-up might result in miscategorization of the site of antibiotic prescribing.

Analyses were conducted in SAS version 9.4 (SAS Institute, Inc, Cary, NC). Deidentified data were used in this analysis, which was determined to be exempt by Harvard Medical School's Institutional Review Board.

RESULTS

In the unmatched sample, there were 5431 index ARI visits to DTC telemedicine, 87 555 to urgent care, and 1 132 116 to PCPs in 2015–2016 that met inclusion criteria. Compared with urgent care and PCP visits, DTC telemedicine visits were more likely to involve children who were older, enrolled in HDHPs, and in the South (Table 1). Among DTC telemedicine visits, 5% were for children <2 years old. At DTC telemedicine visits, children were more likely to receive a diagnosis of viral ARI (68% vs 54% urgent care; 59% PCP visits) or sinusitis (18% vs 8% urgent care; 10% PCP visits) and less likely to receive a diagnosis of otitis media (8% vs 26% urgent care; 23% PCP).

In the unmatched cohort (Table 2), DTC telemedicine visits were associated with substantially increased antibiotic prescribing (52% vs 46% urgent care; 33% PCP; $P < .001$ for both) and decreased guideline-concordant antibiotic management compared with other settings (60% vs 71% urgent care; 80% PCP; $P < .001$ for both).

Antibiotic Prescribing in Matched Visits

After matching, the weighted sample included 4604 DTC telemedicine, 38 408 urgent care, and 485 201 PCP visits with improved balance on observed characteristics, including child age, geographic region, and visit diagnosis (Table 1, Supplemental Table 8).

At DTC telemedicine visits, children were more likely to receive an antibiotic compared with matched visits at other settings (52% vs 42% urgent care; 31% PCP; $P < .001$ for both comparisons; Table 2). At DTC telemedicine visits, children were less likely to receive guideline-concordant antibiotic management (59% vs 67% urgent care; 78% PCP; $P < .001$ for both comparisons). The difference in guideline-concordant antibiotic management rates was primarily driven by antibiotic prescribing for visits with viral ARI diagnoses that do not warrant antibiotics. For such visits, antibiotics were appropriately not prescribed in only 54% of DTC telemedicine visits compared with 66% of urgent care visits ($P < .001$) and 80% of PCP visits ($P < .001$; Table 3).

Streptococcal Testing and Return Visits

In the matched sample, among visits with a diagnosis of streptococcal pharyngitis, streptococcal testing was performed for 4% of DTC telemedicine visits compared with 75% of urgent care and 68% of PCP visits ($P < .001$ for both; Table 4). Subsequent visits within 2 days occurred for a slightly higher percentage of DTC telemedicine visits (5% vs 2% urgent care; 1% PCP; $P < .001$ for both).

Stratified Analysis by Patient Characteristics

Compared with urgent care and PCP visits, DTC telemedicine visits had significantly increased antibiotic prescribing and decreased guideline-concordant antibiotic management within each category of age and chronic medical complexity (Fig 1). The 1 exception was that DTC telemedicine and urgent care results were not statistically different for the youngest children (0–1 year old), for which the sample size was small. Interaction terms indicated that the degree of difference between DTC telemedicine and PCP visits varied significantly with age for antibiotics prescribed (interaction term $P < .001$) and guideline concordance (interaction term $P = .004$); other interaction terms were not significant.

Sensitivity Analyses

When no longer classifying "no antibiotic use" as guideline-concordant for otitis media and sinusitis, rates of guideline-concordant antibiotic management remained lower overall at DTC telemedicine (51% vs 59% urgent care; 69% PCP; $P < .001$ for both; Supplemental Table 9). Analysis excluding index visits with follow-up visits within 2 days did not differ meaningfully from main results.

DISCUSSION

Children treated for ARIs at commercial DTC telemedicine visits were substantially more likely to receive an antibiotic and less likely to receive guideline-concordant antibiotic management than children presenting to urgent care or primary care. These quality differences were observed in metrics agnostic to visit diagnosis (antibiotic prescribing rate) and conditional on diagnosis (guideline-concordant antibiotic management). These differences were primarily driven by increased use of antibiotics for visits receiving viral diagnoses.

These differences in antibiotic prescribing for children contrast with previous studies of DTC telemedicine quality among adult patients in which quality differences have been smaller

TABLE 1 Characteristics of ARI Visits Before and After Matching, 2015–2016

	Pediatric Visits									
	Before Matching					After Matching[a]				
	DTC Telemedicine, No. (%)	Urgent Care, No. (%)	Standardized Difference,[b] %	PCP, No. (%)	Standardized Difference,[b] %	DTC Telemedicine, No. (%)	Urgent Care, No. (%)	Standardized Difference,[b] %	PCP, No. (%)	Standardized Difference,[b] %
Visits, *N*	5431	87 555	—	1 132 116	—	4604	38 408	—	485 201	—
Child age, y										
0–1	245 (5)	8234 (9)	59.0	195 692 (17)	89.6	224 (5)	1956 (5)	4.7	24 192 (5)	2.5
2–5	1305 (24)	24 845 (28)	21.5	390 699 (35)	46.4	1132 (25)	9528 (25)	1.2	121 932 (25)	2.9
6–11	1930 (36)	30 018 (34)	5.6	331 716 (29)	30.1	1614 (35)	13 392 (35)	0.8	168 036 (35)	1.9
12–17	1951 (36)	24 458 (28)	39.3	214 009 (19)	110.7	1634 (35)	13 532 (35)	1.1	171 041 (35)	1.0
Sex										
Female	2755 (51)	44 181 (50)	1.1	555 277 (49)	6.7	2339 (51)	19 513 (51)	0	246 500 (51)	0
Male	2676 (49)	43 374 (50)	—	576 839 (51)	—	2265 (49)	18 895 (49)	—	238 701 (49)	—
Chronic medical complexity[c]										
No chronic conditions	3993 (74)	65 931 (75)	9.5	835 897 (74)	1.6	3542 (77)	29 548 (77)	0	373 280 (77)	0
Noncomplex chronic condition	1062 (20)	14 823 (17)	18.5	197 934 (17)	14.3	803 (17)	6699 (17)	0	84 626 (17)	0
Complex chronic condition	376 (7)	6801 (8)	11.9	98 285 (9)	22.2	259 (6)	2161 (6)	0	27 295 (6)	0
Rural or urban[d]										
Metropolitan	4967 (91)	81 028 (93)	15.7	1 052 233 (93)	22.7	4415 (96)	36 839 (96)	0.5	465 266 (96)	0.1
Micropolitan	284 (5)	4421 (5)	3.7	48 849 (4)	22.1	140 (3)	1161 (3)	0.6	14 771 (3)	0.1
Small town	109 (2)	1449 (2)	21.4	20 540 (2)	10.8	34 (1)	284 (1)	0	3583 (1)	0
Rural	71 (1)	657 (1)	71.7	10 494 (1)	41.3	15 (0)	125 (0)	0	1581 (0)	0
Region										
Northeast	627 (12)	5691 (7)	79.7	346 792 (31)	90.0	490 (11)	4088 (11)	0	51 640 (11)	0
Midwest	929 (17)	16 393 (19)	10.7	161 878 (14)	22.9	701 (15)	5833 (15)	0.3	73 876 (15)	0
South	2943 (54)	42 860 (49)	21.0	445 160 (39)	62.3	2587 (56)	21 757 (57)	1.9	275 657 (57)	2.5
West	932 (17)	22 611 (26)	45.8	178 286 (16)	10.6	826 (18)	6730 (18)	2.9	84 029 (17)	4.3
HDHP										
No	4575 (84)	81 720 (93)	136.2	1 062 214 (94)	164.3	4119 (89)	34 362 (89)	0	434 088 (89)	0
Yes	856 (16)	5835 (7)	—	69 902 (6)	—	485 (11)	4046 (11)	—		—

TABLE 1 Continued

	Pediatric Visits									
	Before Matching					After Matching[a]				
	DTC Telemedicine, No. (%)	Urgent Care, No. (%)	Standardized Difference,[b] %	PCP, No. (%)	Standardized Difference,[b] %	DTC Telemedicine, No. (%)	Urgent Care, No. (%)	Standardized Difference,[b] %	PCP, No. (%)	Standardized Difference,[b] %
									51 113 (11)	
Diagnosis category[e]										
Sinusitis	966 (18)	7101 (8)	122.1	113 392 (10)	85.9	646 (14)	5389 (14)	0	68 080 (14)	0
Streptococcal pharyngitis	326 (6)	11 745 (13)	65.6	103 066 (9)	37.5	250 (5)	2086 (5)	0	26 347 (5)	0
Otitis media	429 (8)	22 838 (26)	96.9	263 743 (23)	86.4	369 (8)	3078 (8)	0	38 888 (8)	0
Viral ARI[f]	3710 (68)	46 979 (54)	59.1	664 912 (59)	39.5	3339 (73)	27 855 (73)	0	351 887 (73)	0

—, not applicable.

[a] Sample characteristics before and after matching. In comparison of matched samples, each stratum of matched sets is weighted to account for differences in the number of matched urgent care and PCP visits. Counts within the matched categories may exceed column total because of rounding of weighted frequencies. Visits were matched by age (in years) and state, but results are reported in the table by larger categories of age group and census region.

[b] Standardized differences comparing the characteristics of urgent care or PCP visits (in the column to the left) to DTC telemedicine, before and after matching.

[c] Patient chronic medical complexity was determined by using the Pediatric Medical Complexity Algorithm applied to all 2014–2016 inpatient and outpatient claims for each patient.[29] This algorithm is used to identify children with 3 levels of chronic medical complexity: complex chronic disease, (ie, significant multisystem chronic disease, progressive conditions with decreased life expectancy, technology dependence, or malignancy), noncomplex chronic disease (ie, chronic conditions such as asthma that do not meet the above criteria), and no chronic disease.

[d] Rural or urban status was determined by using the US Department of Agriculture rural-urban commuting area codes.

[e] Because a small percentage of visits have >1 of these diagnoses (1.1%), percentages for diagnosis category may sum to >100%.

[f] Viral ARI category consists of diagnoses for which antibiotics are not warranted (eg, viral URI, bronchiolitis, viral pharyngitis, and serous otitis media) in the absence of another diagnosis.

or nonexistent.[9,10] For example, using data from the same health plan, we observed similar antibiotic management for adults seeking care for ARIs in these 3 settings.[32] Professional groups such as the American Academy of Pediatrics and the American Telemedicine Association have previously raised concerns about DTC telemedicine care outside of the medical home for pediatric patients.[7,8] Our results support these concerns and underscore the importance of pediatric-specific evaluation and guidelines. Targeted improvement initiatives have the potential to substantially improve the quality of care delivered via DTC telemedicine.[33] Pediatric-specific guidelines and metrics should be incorporated into such efforts.

Several mechanisms could contribute to increased antibiotic prescribing and decreased guideline concordance in pediatric DTC telemedicine visits. First, the potentially rich information that telemedicine can provide in other models of telemedicine, such as when the patient is at a facility designed for telemedicine consultation, is relatively limited in DTC telemedicine. Specifically, the information transmitted in DTC telemedicine is limited in that personal devices used by parents for DTC telemedicine visits rarely incorporate peripheral attachments designed to enhance remote visits (eg, tele-otoscopy) and also do not incorporate trained telepresenters (ie, nurses or medical assistants with the patient). The limited availability of otoscopy and streptococcal testing in DTC telemedicine may contribute to the different diagnosis mix at DTC telemedicine (increased viral ARIs and sinusitis and decreased otitis media and streptococcal pharyngitis) compared with in-person settings. Additionally, personal devices may vary in the quality of microphones, cameras, and Wi-Fi, and some DTC telemedicine visits are completed by

TABLE 2 Antibiotic Prescribing and Guideline-Concordant Antibiotic Management in Matched Sample, 2015–2016

	Unmatched Visits					Matched Visits				
	DTC Telemedicine	Urgent Care	P^a	PCP	P^b	DTC Telemedicine	Urgent Care	P^a	PCP	P^b
Total ARI visits, *N*	5431	87 555	—	1 132 116	—	4604	38 408	—	485 201	—
Any antibiotics prescribed,[c] *n* (%)[d]	2846 (52)	40 594 (46)	<.001	376 638 (33)	<.001	2381 (52)	16 198 (42)	<.001	152 687 (31)	<.001
Guideline-concordant management,[e] *n* (%)[d]	3246 (60)	61 842 (71)	<.001	907 450 (80)	<.001	2712 (59)	25 788 (67)	<.001	376 259 (78)	<.001
Specifics category of guideline concordance and nonconcordance among ARI visits, *n* (%)[d]										
Guideline-concordant use	761 (14)	18 613 (21)	<.001	189 970 (17)	<.001	561 (12)	4260 (11)	.026	52 776 (11)	.005
Guideline nonconcordant use	369 (7)	7514 (9)	<.001	83 297 (7)	.11	271 (6)	2507 (7)	.095	31 138 (6)	.14
Unnecessary antibiotic use	1716 (32)	14 467 (17)	<.001	103 371 (9)	<.001	1549 (34)	9431 (25)	<.001	68 773 (14)	<.001
No antibiotic use	591 (11)	14 449 (17)	<.001	193 937 (17)	<.001	433 (9)	3787 (10)	.33	49 401 (10)	.083
Guideline-concordant nonuse	1994 (37)	32 512 (37)	.54	561 541 (50)	<.001	1790 (39)	18 424 (48)	<.001	283 114 (58)	<.001

—, not applicable.

[a] *P* value determined from χ^2 test for DTC telemedicine versus urgent care visits.

[b] *P* value determined from χ^2 test for DTC telemedicine versus PCP visits.

[c] Visits with antibiotic prescribing include those categorized as guideline-concordant use, guideline nonconcordant use, and unnecessary antibiotic use.

[d] Percentages reported are the proportion of visits in each setting meeting the specified criteria divided by the total number of ARI visits at that setting (indicated by the top row).

[e] Visits with guideline-concordant antibiotic management include those categorized as guideline-concordant antibiotic use, no antibiotic use (for acute otitis media and sinusitis), and guideline-concordant nonuse of antibiotics.

using only telephone. These issues reduce the data available to the treating DTC telemedicine provider, which may be of greater concern in pediatric care because of the more limited ability of children to communicate symptoms. Second, there may be differential expectations for antibiotics among children and parents who use DTC telemedicine versus in-person care. Although we matched on a number of observed variables, parental expectations may still differ across settings in ways that we were unable to address. Third, DTC telemedicine visits outside of the medical home lack 3 types of continuity: informational (lack of medical records), relationship (lack of ongoing relationship between the provider and patient), and clinical management (lack of opportunity to manage the patient's care over time),[34] which has the potential to impact quality of care. However, this is unlikely to be the only explanation given that authors of previous evaluations of retail-based clinics, which are also a model of in-person care with limited continuity, have found comparable quality to physician office visits.[15,19] Fourth, the majority of commercial DTC telemedicine visits are for adults, such that DTC telemedicine providers may have variable pediatric training or experience, which could impact providers' knowledge of and adherence to guideline-based pediatric care.[35] Prior studies indicate that only 9.6% of urgent care centers employ any pediatricians,[36] and pediatricians may also be underrepresented in DTC telemedicine. Together, these issues may increase clinical uncertainty during pediatric DTC telemedicine visits, prompting physicians to prescribe antibiotics "just to be safe."[37,38]

We note additional quality concerns raised by our analysis beyond antibiotic use. First, the American Telemedicine Association has

TABLE 3 Antibiotic Prescribing Outcomes by Diagnosis

	Pediatric Visits				
	DTC Telemedicine	Urgent Care	*P*[a]	PCP	*P*[b]
Total ARI Visits, *N*	4604	38 408	—	485 201	—
Summative categories					
Visits for which antibiotics may be indicated, *n*	1265	10 553	—	133 314	—
Any antibiotic use, *n* (%)	832 (66)	6766 (64)	.25	83 914 (63)	.038
Guideline-concordant antibiotic management,[c] *n* (%)	922 (73)	7364 (70)	.023	93 145 (70)	.020
Sinusitis visits, *n*	646	5389	—	68 080	—
Any antibiotic use, *n* (%)	410 (63)	3415 (63)	.96	43 219 (63)	.99
Guideline-concordant antibiotic management, *n* (%)	471 (73)	3837 (71)	.36	49 611 (73)	.98
Streptococcal pharyngitis visits, *n*	250	2086	—	26 347	—
Any antibiotic use, *n* (%)	178 (71)	1403 (67)	.21	17 315 (66)	.069
Guideline-concordant antibiotic management, *n* (%)	136 (54)	974 (47)	.021	11 424 (43)	<.001
Otitis media visits, *n*	369	3078	—	38 888	—
Any antibiotic use, *n* (%)	244 (66)	1948 (63)	.28	23 380 (60)	.019
Guideline-concordant antibiotic management, *n* (%)	315 (85)	2553 (83)	.24	32 109 (83)	.16
Visits where antibiotics not indicated, *n*	3339	27 855	—	351 887	—
Guideline-concordant antibiotic management, *n* (%)	1790 (54)	18 424 (66)	<.001	283 114 (80)	<.001
Bronchiolitis visits, *n*	51	263	—	4037	—
Guideline-concordant antibiotic management, *n* (%)	31 (61)	182 (69)	.25	3197 (79)	.001
Bronchitis visits, *n*	363	2686	—	27 308	—
Guideline-concordant antibiotic management, *n* (%)	160 (44)	1114 (41)	.344	11 270 (41)	.28
Visits for other viral URIs, *n*	2925	24 906	—	320 542	—
Guideline-concordant antibiotic management, *n* (%)	1599 (55)	17 128 (69)	<.001	268 647 (84)	<.001
Visits where antibiotics prescribed, *n*	2381	16 198	—	152 687	—
Guideline-concordant antibiotic management, *n* (%)	561 (24)	4260 (26)	.005	52 776 (35)	<.001

—, not applicable.

[a] *P* value determined from χ^2 test for DTC telemedicine versus urgent care visits.

[b] *P* value determined from χ^2 test for DTC telemedicine versus PCP visits.

[c] Visits with guideline-concordant antibiotic management include those categorized as guideline-concordant antibiotic use, no antibiotic use (for acute otitis media and sinusitis visits), and guideline-concordant nonuse of antibiotics.

recommended that commercial DTC telemedicine should not be used for children <2 years old.[8] We note that 5% of studied DTC telemedicine visits for ARIs were within this age group but that gaps in quality existed for children of all ages. Second, accurate diagnosis of otitis media in children requires visualization of the tympanic membranes,[11] and accurate diagnosis of streptococcal pharyngitis requires streptococcal testing.[27] Making these diagnoses via telemedicine in the absence of reliable visualization and testing could in itself be considered a quality concern. Third, increased rates of follow-up visits after DTC telemedicine raise questions about the effectiveness and system-level efficiency of these visits.

Quality of care for ARIs may be better in other models of acute telemedicine care. For example, acute telemedicine visits in which peripheral devices such as tele-stethoscopes or tele-otoscopes (such as offered at telemedicine kiosks[39]) are integrated may allow for enhanced examination compared with DTC telemedicine. Using telemedicine technology to connect patients to their PCP's office would allow telemedicine use within the context of continuity of information, relationships, and care management.[7] School-based or day care–based models of acute telemedicine can be used to integrate peripherals and telepresenters.[40,41] Finally, pediatric-specific improvement initiatives may also result in improved quality.[33] Examining the variation in quality across different models of acute telemedicine care may inform optimal use of technology for acute pediatric concerns.

TABLE 4 Streptococcal Testing and Return Visits in Matched Sample, 2015–2016

	Pediatric Visits				
	DTC Telemedicine	Urgent Care	*P*[a]	PCP	*P*[b]
Visits with diagnosis of streptococcal pharyngitis, *N*	250	2086	—	26 347	—
Streptococcal testing performed, *n* (%)	9 (4)	1557 (75)	<.001	17 818 (68)	<.001
Total ARI visits, *N*	4604	38 408	—	485 201	—
Return ARI visit within 2 d, *n* (%)	226 (5)	869 (2)	<.001	5875 (1)	<.001
Return ARI visit within 21 d, *n* (%)	525 (11)	3719 (10)	<.001	45 629 (9)	<.001

—, not applicable.

[a] *P* value determined from χ^2 test for DTC telemedicine versus urgent care visits.

[b] *P* value determined from χ^2 test for DTC telemedicine versus PCP visits.

Although our focus was DTC telemedicine, the quality of antibiotic prescribing was also lower at urgent

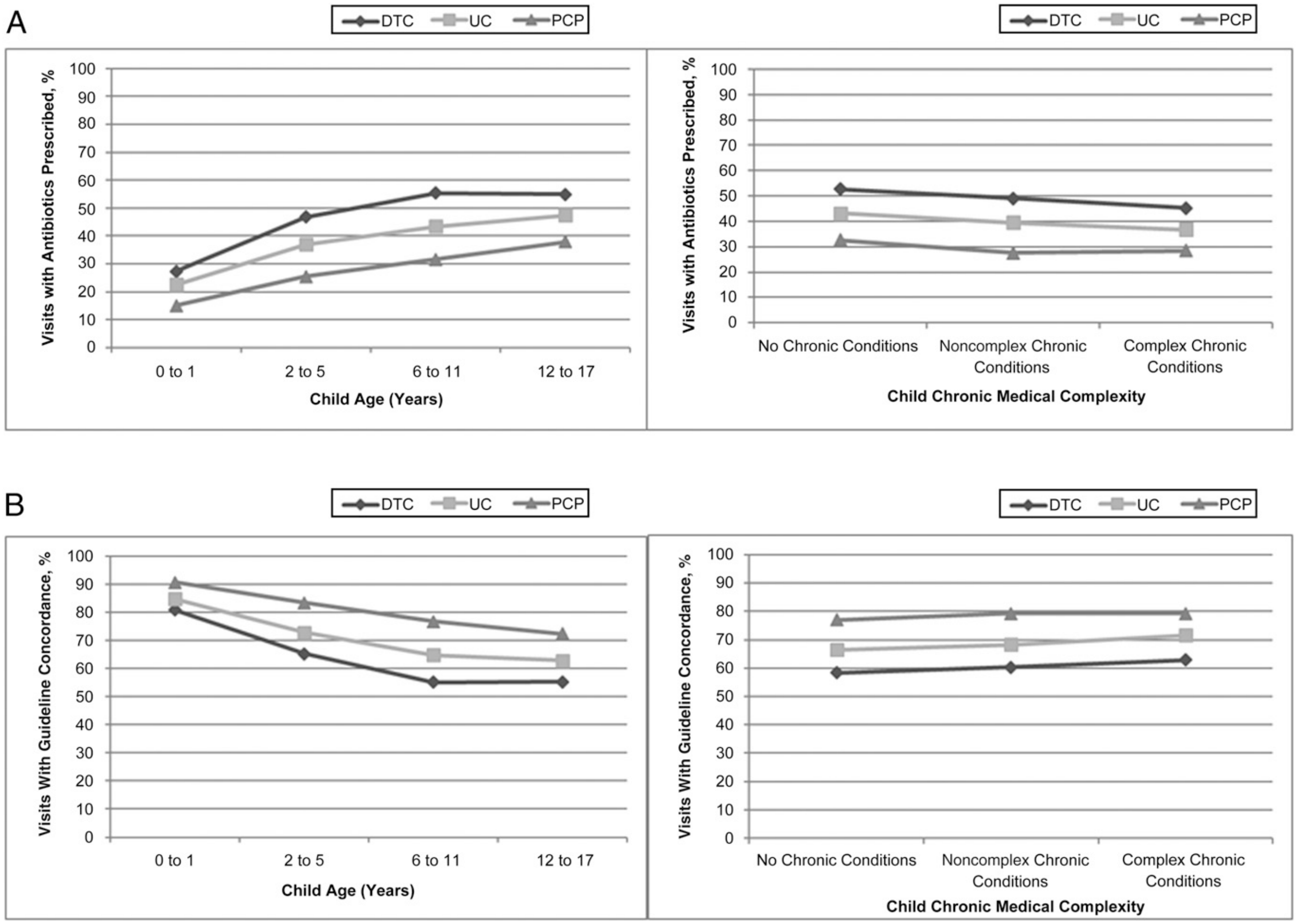

FIGURE 1

Antibiotic prescribing and guideline-concordant antibiotic management for DTC telemedicine compared with urgent care (UC) and PCP visits, stratified by child age and chronic medical complexity. A, Antibiotic prescribing associated with DTC telemedicine visits compared with UC and PCP visits, stratified by 4 levels of child age (left) and 3 levels of chronic medical complexity (right). B, Guideline-concordant antibiotic management associated with DTC telemedicine visits compared with UC and PCP visits, stratified by 4 levels of child age (left) and 3 levels of chronic medical complexity (right). Within each age or medical complexity category, the values for UC and PCP visits differed significantly from DTC telemedicine with 1 exception: DTC telemedicine and UC results were not statistically different for the youngest children (0–1 year old). Interaction terms indicated that the degree of difference between DTC telemedicine and PCP visits varied significantly with age for antibiotics prescribed (interaction term $P < .001$) and guideline concordance (interaction term $P = .004$); other interaction terms were not significant.

care visits compared with PCP visits (59% vs 67% guideline concordant). Urgent care clinics have grown rapidly in the United States,[42] and urgent care and DTC telemedicine share some characteristics that might impede quality, such as limited continuity. Across all 3 settings, our findings emphasize the need for improvement in guideline-concordant antibiotic use and ongoing antibiotic stewardship efforts in outpatient settings.[43–48]

Our analysis had several limitations. As an analysis of insurance claims, we did not have additional sociodemographic or clinical data and thus could not account for variables such as patient race, severity of illness, time constraints, or family expectations, which might drive differences in prescribing.[38,49] Given the data available, we could not independently confirm the diagnosis made. The differences in diagnosis mix in the unmatched data could be due to true differences in case mix (perhaps due to self-selection to specific settings on the part of parents) or biases in diagnosis (perhaps due to differences in information available to clinicians or differences in desire to select a diagnosis that justifies prescription of antibiotics). Insurance claims also do not have information on patient allergies. Although we would not expect substantial differences in rates of allergies across settings, we may be underestimating overall guideline concordance in the absence of allergy data. Also, because some children were enrolled for brief periods, we may not be capturing all children with higher medical complexity. However, we confirmed that identified rates of chronic complex disease in the full population of pediatric health plan beneficiaries (6.4%) were relatively similar to rates identified in other population studies (6% in previous claims analysis[29]). We used claims data rather than electronic health record or provider-reported data. Although this means we examined antibiotics filled rather than prescribed, in-person visit antibiotic use appeared consistent with previous studies of antibiotic use. Specifically, our rates of antibiotic use among unmatched PCP visits were comparable to previous studies for diagnoses for which antibiotics may be indicated (59% vs 50%–80% in previous literature) and diagnoses for which antibiotics are not indicated (16% vs 20%–21% in previous literature).[14,20,50] We did not include retail-based clinics in our analyses. Authors of other studies have found that among adults, retail-based clinics have higher rates of guideline-concordant care relative to PCPs.[15,19] Physician specialty was not available for DTC telemedicine visits, so we could not examine whether pediatric-specific physician training explained any quality differences. We note also that our analysis is limited to a specific health plan and visits by its members to their contracted DTC telemedicine vendor, and our analysis also did not include Medicaid beneficiaries. Antibiotic prescribing among other DTC telemedicine companies, models, and populations may differ. Understanding the impact of physician training and telemedicine models on quality of care during DTC telemedicine should be a priority in future work.

CONCLUSIONS

Children who receive care via DTC telemedicine visits were significantly more likely to receive antibiotics and less likely to receive guideline-concordant antibiotic management than children who visit either urgent care or PCPs.

ABBREVIATIONS

ARI: acute respiratory infection
DTC: direct-to-consumer
HDHP: high-deductible health plan
ICD-9-CM: *International Classification of Diseases, Ninth Revision, Clinical Modification*
ICD-10-CM: *International Classification of Diseases, 10th Revision, Clinical Modification*
PCP: primary care provider
URI: upper respiratory infection

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Sleep-Related Infant Suffocation Deaths Attributable to Soft Bedding, Overlay, and Wedging

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abstract

BACKGROUND: Unintentional suffocation is the leading cause of injury death among infants <1 year old in the United States, with 82% being attributable to accidental suffocation and strangulation in bed. Understanding the circumstances surrounding these deaths may inform prevention strategies.

METHODS: We analyzed data from the population-based Sudden Unexpected Infant Death Case Registry from 2011 to 2014. Cases categorized as explained suffocation with unsafe sleep factors (suffocation), per the Centers for Disease Control and Prevention's Sudden Unexpected Infant Death Case Registry classification system, were included and assigned a mechanism of obstruction, including soft bedding, overlay, or wedging. We calculated frequencies and percentages of suffocation deaths by mechanism and selected demographic and sleep-environment characteristics.

RESULTS: Fourteen percent of sudden unexpected infant death cases were classified as suffocation; these cases were most frequently attributed to soft bedding (69%), followed by overlay (19%) and wedging (12%). Median age at death in months varied by mechanism: 3 for soft bedding, 2 for overlay, and 6 for wedging. Soft-bedding deaths occurred most often in an adult bed (49%), in a prone position (82%), and with a blanket (or blankets) obstructing the airway (34%). Overlay deaths occurred most often in an adult bed (71%), and infants were overlaid by the mother (47%). Wedging deaths occurred most often when the infant became entrapped between a mattress and a wall (48%).

CONCLUSIONS: Safe sleep environments can reduce infant suffocation deaths. Increased knowledge about the characteristics of suffocation deaths can help inform prevention strategies by targeting highest-risk groups.

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Ms Erck Lambert conceptualized and designed the study, conducted all analyses, drafted the initial manuscript, and reviewed and revised the manuscript; Drs Parks, Hauck, and Shapiro-Mendoza, Ms Cottengim, and Ms Faulkner conceptualized and designed the study and critically reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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WHAT'S KNOWN ON THIS SUBJECT: Unintentional suffocation is the leading cause of injury death among US infants, with 82% attributable to accidental suffocation and strangulation in bed. These deaths are preventable. In Sudden Unexpected Infant Death Case Registry data, airway obstruction is differentiated by mechanism.

WHAT THIS STUDY ADDS: Soft-bedding deaths occur more than overlay and wedging deaths. Suffocation by pillows occurs twice as often among infants ≤4 months old. If suffocation deaths had been prevented during the study period, the US sudden unexpected infant death rate would have dropped below the Healthy People 2020 goal.

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Unintentional suffocation is the leading cause of injury death among infants (<1 year old) in the United States.[1] Eighty-two percent of unintentional infant suffocation deaths are attributed to accidental suffocation and strangulation in bed (ASSB). According to US death-certificate data, rates of infant deaths reported as ASSB per 100 000 live births have increased nearly fourfold, from 6 deaths in 1999 to 23 deaths in 2015.[2] This increase is at least partly attributed to changing diagnostic preferences and improved death investigations.[2] These injury deaths, often resulting from hazards in the sleep environment, are preventable. Historically, surveillance of infant sleep-related suffocation deaths has relied on underlying cause-of-death codes that are assigned on the basis of the cause of death from death certificates. However, death certificates do not systematically collect information about the circumstances of death. Differentiating a death caused by suffocation from other causes of sudden unexpected infant death (SUID), such as sudden infant death syndrome (SIDS), relies on detailed information from the death-scene investigation and autopsy, for which practices are not standard across jusridictions.[3] Furthermore, variations are known to exist in diagnostic preferences and the levels of evidence death certifiers use to designate suffocation as a cause of death, leading to a diagnostic shift in SUID from SIDS to ASSB.[2–5]

In 2009, the Centers for Disease Control and Prevention (CDC) created the Sudden Unexpected Infant Death Case Registry to better understand the trends and characteristics associated with SUID, including sleep-related suffocation.[6] The SUID Case Registry is built on existing Child Death Review programs and the National Center for Fatality Review and Prevention protocols and data system.[7] The Case Registry is a multijurisdictional, population-based surveillance system that monitors SUID cases using data from death-scene investigations, autopsies, medical records, and other relevant data sources. Approximately one-third of US SUID cases are captured in the Case Registry. States participating in the Case Registry receive assistance from the CDC to improve data quality, timeliness, and case ascertainment.

In 2014, the CDC developed the Case Registry classification system to consistently differentiate SUID cases into the following groups: no autopsy or death-scene investigation, incomplete case information, no unsafe sleep factors, unsafe sleep factors, possible suffocation with unsafe sleep factors, and explained suffocations with unsafe sleep factors.[8] To understand the factors contributing to and mechanisms of suffocation deaths, the classification system requires the review of detailed information about specific circumstances of each death, including the sleep location and position when found. This information and the resulting classification are important to reliably monitor the incidence of and trends in SUID and SUID subtypes. Identifying factors contributing to suffocation deaths occurring in unsafe sleep environments addresses national and international research priorities[9] and may help inform strategies to reduce these deaths. In this study, we describe demographic and sleep-environment characteristics of SUID cases classified as explained suffocation with unsafe sleep factors (suffocation) per the CDC's SUID Case Registry classification system. This classification requires a high level of evidence of airway obstruction, which is described in detail below.

METHODS

Using data from the CDC's SUID Case Registry,[6] we analyzed infant deaths that occurred from 2011 through 2014 (the most recent year for which categorized Case Registry data were available) among residents of states participating in the Case Registry. Infants were defined as children <1 year old. We limited the study population to deaths classified as suffocation per the classification system.[8] Data were derived from the states participating in the Case Registry at the time of this study, including Arizona, Colorado, Georgia, Louisiana, Michigan, Minnesota, New Hampshire, New Jersey, New Mexico, and Wisconsin. In addition to existing data-use agreements, all states agreed to the use of their deidentified aggregate data for this study.

For these analyses, the authors classified Case Registry cases using the classification system. Cases were classified as suffocation when all of the following criteria were met.[8] First, the reported cause on the death certificate was one of the following: unknown; undetermined; SIDS; SUID; unintentional sleep-related asphyxia, suffocation, or strangulation; unspecified suffocation; cardiac or respiratory arrest without other well-defined causes; or ill-defined causes with potentially contributing unsafe sleep factors. Intentional homicides were excluded. Second, a complete death investigation documented where and how the infant was found, and a comprehensive autopsy included (at a minimum) toxicology, imaging, and pathology. Third, the infant was found unresponsive in an unsafe sleep environment with a reliable, nonconflicting witness account of a full external airway obstruction of both the nose and mouth or airway obstruction due to compression of the neck and/or chest. Finally, there were no other potentially fatal findings or concerning conditions (eg, sepsis or congenital birth defect) reported.

Using the classification system, the authors assigned each suffocation case 1 or more mechanisms to which the airway obstruction was attributed. Mechanisms included soft bedding, overlay, wedging, and other.[8] Soft bedding was assigned when an infant's airway was obstructed by an adult mattress, blanket, pillow, couch cushion, or other soft object in the immediate sleep environment. Wedging was assigned when an infant's airway was obstructed as the result of being trapped or compressed between inanimate objects (eg, a mattress and wall). Overlay was assigned when there was a witnessed account of a person on top of or against an infant, obstructing the infant's airway. Other was assigned only when the airway obstruction was caused by something in the sleep environment other than soft bedding, overlay, or wedging, such as a plastic bag. Cases could have been assigned >1 mechanism. For example, an infant whose nose and mouth were obstructed by soft bedding (soft bedding), and had his or her neck or chest compressed by a person (overlay).

We derived study variables from individual fields in the National Center for Fatality Review and Prevention's National Fatality Review Case Reporting System by combining information from different fields or after a qualitative review of written text.[10] Selected variables were those most pertinent to the study question with the most complete information recorded. This study includes infants from birth to <1 year old. Age is reported in completed months. For example, 0 months includes infants from birth to <1 month old, and 11 months includes infants from 11 to <12 months old. Medicaid is a state and/or federal health insurance program for people with low income and is used as a proxy for socioeconomic status. Qualitative variables include object obstructing the airway, person sharing the sleep surface with the infant, person who overlaid the infant, body part that overlaid the infant, airway obstruction type, person who overlaid was impaired by drugs or alcohol near the time he or she went to sleep with the infant, and objects infant was wedged between. In cases in which the object that obstructed the airway was an adult mattress, there may have been sheets, blankets, or other bedding materials between the adult mattress and the infant's airway. We calculated frequencies and percentages of suffocation by mechanism and selected variables, including infant demographics and sleep-environmental factors at the time of death. Per the data-use agreement with states, counts of 1 through 2 are suppressed in an effort to protect confidentiality. Analyses were conducted by using SAS for Windows version 9.3 (SAS Institute, Inc, Cary, NC).

RESULTS

Of 1812 cases in the Case Registry from 2011 through 2014, 250 (14%) were classified as suffocation per the classification system; the remaining cases were classified as unexplained SUID. Of suffocation cases, 219 were assigned 1 mechanism, and 31 were assigned 2 mechanisms. Cases with 2 mechanisms were counted in both mechanism groups; thus, 281 mechanisms were assigned to the 250 cases. Seven cases were assigned the mechanism other. The majority of these infants were suffocated by plastic bags. Because of the small size of this group, these cases are not included in the analyses by mechanism. Of the mechanisms assigned, 190 (69%) were soft bedding, 51 (19%) were overlay, and 33 (12%) were wedging (Table 1).

A majority of infants were boys, born at term (≥37 weeks' gestation), non-Hispanic white or African American, and insured by Medicaid (Table 1). The median age at death was 3 months, and most deaths occurred in the infant's home. The distribution of age at death varied by mechanism (Fig 1). Among soft-bedding deaths, 68% occurred from 1 through 4 months old (median = 3 months old). Among overlay deaths, 71% occurred during the first 2 months of life (median = 2 months), and no deaths occurred after 7 months. More than half (58%) of wedging deaths occurred from 5 through 8 months old (median = 6 months old). Of the 51 suffocation deaths attributed to overlay, 25% were born preterm (<37 weeks' gestation) compared with 15% among soft bedding and 12% among wedging. Also, 49% of overlay deaths were exposed to prenatal maternal smoking compared with 36% among soft bedding and 27% among wedging.

Soft Bedding

Suffocation deaths attributed to soft bedding varied by sleep place, position found, surface-sharing status, and type of object obstructing the airway (Table 2). Among soft-bedding deaths, 49% occurred in an adult bed, and 27% occurred in a crib or bassinet (including portable cribs; Table 2). Most (92%) were found in a nonsupine position. Of the 92 infants (48%) who were found sharing a sleep surface with another person, 61 (66%) were sharing with 1 or both parents, and 24 (26%) were sharing with 1 or more siblings (these groups are not mutually exclusive, nor are data shown in tables). Of the soft objects reported as obstructing the infants' airways, 34% were blankets, 23% were adult mattresses, and 22% were pillows.

The type of object obstructing the airway differed by infant age. Infants ≤4 months old had their airways obstructed by pillows or couch or recliner cushions approximately twice as often as infants 5 to 11 months old (25% vs 11% for pillows; 12% vs 7% for couch or recliner cushions). Infants 5 to 11 months old had their airways obstructed by blankets approximately twice as often as infants ≤4 months old (55% vs 27%).

TABLE 1 Selected Characteristics of Suffocation Deaths Overall (*n* = 250) and by Mechanism (*n* = 274): 2011–2014

	Overall		Soft Bedding		Overlay		Wedging	
	n	%	*n*	%	*n*	%	*n*	%
Overall	250		190	69	51	19	33	12
Infant sex								
Male	137	55	104	55	26	51	17	52
Female	112	45	85	45	25	49	16	48
Missing	a	a	a	a	a	a	a	a
Gestational age at birth, wk								
Preterm, <37	41	16	28	15	13	25	4	12
Term, ≥37	202	81	156	82	37	73	28	85
Missing	7	3	6	3	a	a	a	a
Infant race and/or ethnicity								
Non-Hispanic white	101	40	75	39	22	43	13	39
Non-Hispanic African American	85	34	59	31	22	43	13	39
Hispanic	41	16	36	19	4	8	a	a
Other, missing, or unknown	23	9	20	11	3	6	a	a
Infant insured by Medicaid								
Yes	176	70	130	68	44	86	19	58
No	44	18	36	19	3	6	7	21
Unknown	30	12	24	13	4	8	7	21
Location of death								
Infant's home	209	84	154	81	45	88	28	85
Friend's or relative's home	24	10	21	11	3	6	3	9
Day care	7	3	6	3	a	a	a	a
Missing or other	10	4	9	5	a	a	a	a
Exposure to prenatal maternal smoking								
Yes	89	36	69	36	25	49	9	27
No	138	55	104	55	19	37	21	64
Unknown	23	9	17	9	7	14	3	9

The overall column includes all 250 suffocation cases; cases assigned 2 mechanisms are included in the total for each of the assigned mechanisms.

[a] Per the data-use agreement with states, counts of 1 through 2 are suppressed in an effort to protect confidentiality.

Overlay

Seventy-one percent of overlay deaths occurred in an adult bed, and 51% were found nonsupine (Table 3). Of persons who overlaid these infants, 47% were the mother, 25% were the father, and 22% were a sibling. In 41% of the overlay deaths, the infant was sharing a sleep surface with >1 person. Among overlay deaths, 7 (14%) were overlaid by the mother's breast (data not shown in tables). Most overlay deaths (71%) were attributed to neck or chest compression as opposed to obstruction of the nose and mouth (22%) or both or unknown (8%). Of the 40 overlay deaths in which an adult overlaid the infant, 23% of the adults were reported to have been impaired by alcohol or drugs around the time they went to sleep with the infant. Among the 10 overlay deaths that occurred after an adult fell asleep while feeding the infant, 7 were breastfeeding (14% of all overlay deaths).

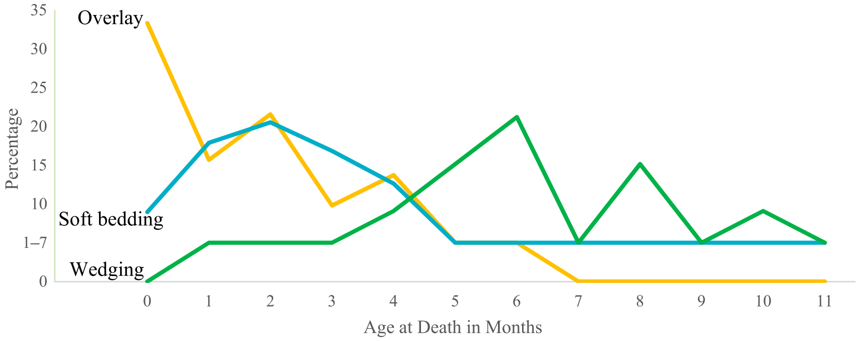

FIGURE 1
Age distribution for each mechanism of suffocation death (2011–2014; *n* = 274). In an effort to protect confidentiality and per the data-use agreement with states, percentages in the 1% to 7% range with a numerator of 1 through 2 are all shown on the y-axis at the same level (5%).

Wedging

Of the 33 suffocation deaths attributed to wedging, 45% were sharing a sleep surface at the time of death, and 73% occurred in an adult bed (Table 4). The objects between which the infant was wedged were most frequently a mattress and wall (48%), followed by a mattress and bed frame (including headboard; 27%). Some infants were wedged between a crib mattress and something else; these cases all involved a crib mattress used with a broken crib or a crib mattress that

TABLE 2 Suffocation Soft-Bedding Deaths by Age at Death and Sleep Circumstances (*n* = 190): 2011–2014

	All Ages		0–4 mo		5–11 mo	
	n	%	*n*	%	*n*	%
Sleep place						
Adult bed	93	49	71	49	22	50
Crib or bassinet	51	27	41	28	10	23
Chair or couch	26	14	22	15	4	9
Other	20	11	12	8	8	18
Position found						
Prone	155	82	126	86	29	69
Side	19	10	10	7	9	21
Supine	14	7	10	7	4	10
Sharing a sleep surface with another person						
No	95	50	69	47	26	59
Yes	92	48	75	51	17	39
Unknown	3	2	[a]	[a]	[a]	[a]
Object obstructing airway						
Blanket(s)	64	34	40	27	24	55
Adult mattress	44	23	35	24	9	20
Pillow	42	22	37	25	5	11
Couch or recliner cushion	20	11	17	12	3	7
Multiple objects	10	5	[a]	[a]	[a]	[a]
Bumper pad	5	3	[a]	[a]	[a]	[a]
Other	5	3	5	3	0	0

Groups do not equal 100% because of rounding.

[a] Per the data-use agreement with states, counts of 1 through 2 are suppressed in an effort to protect confidentiality.

was ill fitting or not used as recommended (eg, an infant between a crib mattress and an adult mattress that were both placed on the floor or an infant between a crib mattress and the broken rail of a drop-down crib).

DISCUSSION

From 2011 to 2014, 250 of 1812 (14%) Case Registry cases were classified as suffocation as defined by the classification system.[8] Suffocation deaths were most frequently attributed to an airway obstruction by soft bedding, followed by overlay and wedging. These deaths represent a small proportion of all SUID cases, but safe sleep environments can prevent suffocation deaths. From 2011 to 2014, the US SUID rate was 87 deaths per 100 000 live births, according to National Center for Health Statistics data.[11] If the number of deaths proportionally equivalent to the 14% of Case Registry cases classified as suffocation from 2011 through 2014 had been prevented, the US SUID rate would have dropped to 75 deaths per 100 000 live births, which is below the Healthy People 2020 goal of 84.[11,12]

Our study revealed the following commonalities and differences in characteristics of suffocation deaths stratified by mechanism of airway obstruction. Nonsupine sleep position and sleeping in an adult bed were common characteristics among deaths attributed to all 3 mechanisms. Soft-bedding deaths most commonly involved an airway obstruction by blankets. Among overlay deaths, surface sharing with the parent(s) was most common, and infants were most often overlaid by their mothers. Wedging deaths most frequently occurred when the infant became stuck between an adult mattress and a wall.

Our findings reveal that factors and mechanisms of suffocation differ by infant age. Younger infants (≤4 months old) were more often suffocated by overlay or soft bedding than wedging. Younger infants are less likely to get themselves into a wedged position because they are less mobile and cannot roll over on their own. Infants who were suffocated by overlay were youngest and had a higher proportion born preterm than infants who were suffocated by soft bedding or via wedging.

Among soft-bedding deaths, more than half of infants 5 to 11 months old had their airways obstructed by blankets compared with less than one-third of younger infants. Almost half of infants 5 to 11 months old whose airways were obstructed by blankets were entangled in the blankets. It is likely that these older, more developed infants were mobile enough to become entangled in blankets but were not yet coordinated enough to free themselves. Pillows caused the airway obstructions twice as often among infants ≤4 months old compared with infants 5 to 11 months old. Younger infants may have lacked the mobility and neck strength necessary to lift their heads to prevent an airway obstruction, especially when placed prone or on their side on a pillow.[13]

TABLE 3 Suffocation Overlay Deaths by Sleep Circumstances (*n* = 51): 2011–2014

	Age at Death 0–6 mo[a]	
	n	%
Sleep place		
Adult bed	36	71
Chair or couch	13	25
Crib or bassinet	[b]	[b]
Other	[b]	[b]
Found position		
Prone	14	27
Side	12	24
Supine	25	49
Person involved with overlay		
Mother	24	47
Father	13	25
Sibling	11	22
Other	3	6
Airway obstruction mechanism		
Neck or chest compression	36	71
Nose and mouth obstruction	11	22
Unknown or both	4	8
Adult fell asleep feeding the infant		
No or unknown	41	80
Yes	10	20
Feeding type among adults who fell asleep feeding the infant (*n* = 10)[c]		
Breast	7	70
Bottle	3	30
Person who overlaid impaired by drugs or alcohol (*n* = 40)[d]		
Yes	9	23
No, not specified, or unknown	31	78

Groups do not equal 100% because of rounding.

[a] There were no deaths after 6 mo of age.

[b] Per the data-use agreement with states, counts of 1 through 2 are suppressed in an effort to protect confidentiality.

[c] Denominator = adults who fell asleep feeding.

[d] Denominator = adult or nonsibling overlays.

The American Academy of Pediatrics (AAP) recommends that infants sleep supine in a safety-approved crib, bassinet, or portable crib with no soft objects or bedding in the sleep area.[14] The AAP also recommends that infants share a room but not a sleep surface.[14] Following the AAP safe-sleep recommendations can prevent suffocation deaths.

Despite differences in case inclusion criteria, definitions, and the process of assigning cause of death and mechanism, some of our findings are consistent with earlier studies examining infant sleep-related suffocation deaths.[15–20] Among suffocation deaths, there was a higher proportion of younger infants.[15–17] Overlay deaths were more common among infants 0 to 2 months old, and wedging deaths were more common among infants 3 to 6 months old.[17] Pillows, mattresses, and blankets or comforters were the most common objects obstructing infant airways.[15] As in our study, most overlay deaths occurred on an adult bed or couch,[17,18] and infants were most often overlaid by a parent or sibling.[16,18] Although an infrequent occurrence, other studies have also reported overlay deaths when the infant's mother fell asleep breastfeeding.[16] Wedging deaths most commonly occurred between a mattress or bed and wall,[15–18] and those that occurred in a crib were related to an ill-fitting mattress or faulty crib.[16,17,19]

TABLE 4 Suffocation Wedging Deaths by Sleep Circumstances (*n* = 33): 2011–2014

	n	%
Sleep place		
Adult bed	24	73
Crib or bassinet	4	12
Other (including chair or couch)	5	15
Sharing a sleep surface with another person		
No	17	52
Yes	15	45
Unknown	[a]	[a]
Objects infant was wedged between		
Mattress and wall	16	48
Mattress and bed frame	9	27
Crib mattress and other	[a]	[a]
Other (eg, in a stroller or between ottoman and couch)	[a]	[a]

[a] Per the data-use agreement with states, counts of 1 through 2 are suppressed in an effort to protect confidentiality.

Our analyses were subject to some limitations. A high level of detailed evidence about the circumstances at death was required to be categorized as suffocation with the classification system. As a result, there may have been infants included in the Case Registry during the study years who were suffocated by hazards in their sleep environments, but the death investigation or documentation lacked the evidence necessary for the case to be categorized as suffocation. Like earlier SUID studies, information about a surface sharer's drug and alcohol impairment was not documented consistently.[21,22] Furthermore, because this was a descriptive study of a population of infants who died, we lacked a comparison group and thus were unable to quantify risk associated with infant sleep practices (ie, there was no control group). Also, the size of the study population limited our ability to make meaningful observations about some of the smaller groups in our stratified analyses.

Despite these limitations, our data source and the resulting analyses have several strengths. Case Registry states committed to conducting population-based SUID surveillance and received targeted assistance and resources from the CDC to improve data quality and completeness.[6,7] Earlier studies have used data derived from the National Fatality Review Case Reporting System without restricting cases to those from Case Registry states and thus have had less complete data.[23–25] The strengths of Case Registry data address the limitations of other available data sources, such as death certificates. Studies using only death-certificate data lack specifics about the sleep environment and are limited by inconsistent classification of suffocation deaths. Case Registry data include detailed information about the sleep environment, allowing for classification on the basis of strong evidence of suffocation by using standardized criteria and definitions[8] and the differentiation of airway obstruction by mechanism. Finally, because complete and comprehensive data about the sleep environment were required to classify a case as suffocation, there were no missing and unknown responses for any sleep-environment variables.

CONCLUSIONS

Since 1999, there has been a dramatic increase in the number of US infant deaths attributed to suffocation. These observed rates may not be fully explained by increased incidence and are at least partly attributed to changing diagnostic preferences and improved death investigations.[2] Regardless, unintentional injury deaths, such as those categorized as suffocation in our study, can be prevented by following infant safe-sleep practices. The safest place for infants to sleep is on their backs, on an unshared sleep surface, in a crib or bassinet in the caregivers' room, and without soft bedding (eg, blankets, pillows, and other soft objects) in their sleep area.[14] Improving our understanding of the characteristics and risk factors (eg, age differences and sleep-environment characteristics) of suffocation deaths by mechanism of airway obstruction can inform the development of more targeted strategies to prevent these injuries and deaths.

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ABBREVIATIONS

AAP: American Academy of Pediatrics
ASSB: accidental suffocation and strangulation in bed
CDC: Centers for Disease Control and Prevention
SIDS: sudden infant death syndrome
SUID: sudden unexpected infant death

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Sleep-Related Infant Suffocation Deaths Attributable to Soft Bedding, Overlay, and Wedging

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Accuracy of Autism Screening in a Large Pediatric Network

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abstract

BACKGROUND: Universal screening is recommended to reduce the age of diagnosis for autism spectrum disorder (ASD). However, there are insufficient data on children who screen negative and no study of outcomes from truly universal screening. With this study, we filled these gaps by examining the accuracy of universal screening with systematic follow-up through 4 to 8 years.

METHODS: Universal, primary care-based screening was conducted using the Modified Checklist for Autism in Toddlers with Follow-Up (M-CHAT/F) and supported by electronic administration and integration into electronic health records. All children with a well-child visit (1) between 16 and 26 months, (2) at a Children's Hospital of Philadelphia site after universal electronic screening was initiated, and (3) between January 2011 and July 2015 were included ($N = 25\,999$).

RESULTS: Nearly universal screening was achieved (91%), and ASD prevalence was 2.2%. Overall, the M-CHAT/F's sensitivity was 38.8%, and its positive predictive value (PPV) was 14.6%. Sensitivity was higher in older toddlers and with repeated screenings, whereas PPV was lower in girls. Finally, the M-CHAT/F's specificity and PPV were lower in children of color and those from lower-income households.

CONCLUSIONS: Universal screening in primary care is possible when supported by electronic administration. In this "real-world" cohort that was systematically followed, the M-CHAT/F was less accurate in detecting ASD than in previous studies. Disparities in screening rates and accuracy were evident in traditionally underrepresented groups. Future research should focus on the development of new methods that detect a greater proportion of children with ASD and reduce disparities in the screening process.

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Dr Guthrie conceptualized and designed the study, performed data analysis and interpretation, and drafted the initial manuscript; Drs Wallis and Miller contributed substantially to the study design and helped to draft the initial manuscript; Ms Brooks and Ms Dudley contributed substantially to data acquisition; Dr Gerdes contributed substantially to the study design, data acquisition, and interpretation; Drs Bennett, Levy, Pandey, and Schultz contributed substantially to the study design and data interpretation; and all authors reviewed and revised the manuscript, approved the final manuscript as submitted, and agree to be accountable for all aspects of the work.

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WHAT'S KNOWN ON THIS SUBJECT: Universal screening for autism spectrum disorder is recommended in primary care to facilitate early detection. However, the US Preventive Services Task Force concluded that there is currently insufficient data from primary care and with longitudinal follow-up to recommend universal screening.

WHAT THIS STUDY ADDS: We examined the accuracy of autism screening in a diverse cohort screened nearly universally (91%) and followed-up systematically. The M-CHAT/F had lower sensitivity and positive predictive value than in previous studies; disparities were observed in screening rates and accuracy.

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Although autism spectrum disorder (ASD) manifests in the first few years of life, the average age of diagnosis remains older than 4 years of age[1] and is even later for children of color and those from rural and lower-income backgrounds.[2,3] Improving early diagnosis is critical because it affords children access to earlier intervention, which has been shown to significantly improve outcomes.[4–6] The American Academy of Pediatrics (AAP)[7] recommends universal screening for ASD at 18 and 24 months to facilitate earlier identification. However, the US Preventive Services Task Force concluded that there is insufficient evidence to recommend universal screening, in part because of limited data on outcomes for children who screen negative and from diverse samples. Coupled with the lack of data on truly universal screening (ie, all children are screened rather than a selected subset), there are critical gaps in knowledge about the short- and long-term benefits of universal ASD screening.[8]

The most widely used and studied screening tool is the Modified Checklist for Autism in Toddlers with Follow-Up (M-CHAT/F),[9,10] a 2-stage tool that includes a 23-item parent questionnaire and a follow-up interview designed to reduce false-positives. The Modified Checklist for Autism in Toddlers, Revised, with Follow-Up (M-CHAT–R/F), reworded and removed items and introduced new scoring criteria that recommend bypassing the follow-up interview for scores of 8+. M-CHAT/F and M-CHAT–R/F data are frequently combined because M-CHAT–R/F scoring criteria can be applied to M-CHAT/F administrations, and accuracy is comparable across versions.[9] Estimates of positive predictive value (PPV) for the M-CHAT/F and M-CHAT–R/F have varied widely (2%–65%) depending in part on the sample's ASD prevalence.[9,11–13] However, PPV is optimized when the follow-up interview is used.[11] There are few sensitivity, specificity, or negative predictive value (NPV) estimates because these require systematic follow-up of all children, including those who screen negative.

To date, 2 large-scale studies have been used to conduct systematic, longitudinal follow-up of the Modified Checklist for Autism in Toddlers without Follow-Up (M-CHAT). However, both have important limitations that restrict generalizability. A study conducted in Malaysian maternal-child health clinics yielded only a 0.2% screen-positive rate in a sample with a 0.3% ASD prevalence rate.[14] A large study of population screening in Norway yielded a higher screen-positive rate (7.4%), but the ASD prevalence was still low (0.3%), suggesting that the study's methods failed to detect many children with ASD.[15] Despite large sample sizes, neither study achieved universal screening (ie, 65% and ~28%, respectively).[14,15] Although there are limitations, these first estimates in samples that were systematically followed-up suggested low sensitivity and PPV (34%–36% and 2%–47%, respectively).

It is critical to assess screening accuracy within the intended population (eg, all children in a primary care population) to reduce bias and facilitate the generalization of findings to similar cohorts. Sensitivity and specificity are often presumed to be fixed and inherent to the measure, but in reality, these measures are strongly influenced by the sample and/or cohort in which they are estimated.[16] Samples that are not ascertained through universal screening are likely to overrepresent children with parent and/or professional concern and/or underrepresent children of color and those from lower-income households. In addition, PPV and NPV are directly linked to the sample's prevalence rate, such that PPV increases and NPV decreases with prevalence.[16] Thus, without universal screening research and representative cohorts, we risk drawing incorrect conclusions about the accuracy of screening tools in real-world applications.

Our goal with this study was to examine the real-world accuracy of universal screening for ASD by using an epidemiological design and long-term follow-up through 4 to 8 years of age. Screening was conducted at the Children's Hospital of Philadelphia (CHOP), a large pediatric network of primary and specialty care services with an integrated electronic health record (EHR). Our secondary goals were to examine the accuracy of repeated screenings and the effect of child and/or family characteristics on screening rates and accuracy.

METHODS

Setting

The CHOP network includes 31 pediatric primary care sites that serve a diverse patient population in Pennsylvania and New Jersey. Of these, 4 sites in urban Philadelphia serve a racially and economically diverse patient population (88% children of color, 74% public insurance/Medicaid), wheras suburban sites are less diverse (35% children of color, 24% public insurance/Medicaid).

The M-CHAT/F is administered electronically at well-child visits between 16 and 26 months in accordance with Pennsylvania's Early and Periodic Screening, Diagnostic, and Treatment program[17] and is available in English and Spanish. Screening is automatically triggered at all well-child visits in this age range, regardless of previous screening results, to ensure that children are screened twice as recommended by the AAP. Given that not all children present for 18- and

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24-month well-child visits, the M-CHAT/F can also be assessed manually at sick visits. Once the M-CHAT/F is completed, questionnaire results autopopulate into the child's visit note along with a link for providers to complete the follow-up interview when children screen positive.

CHOP provides ASD diagnostic services through a multidisciplinary program that includes developmental pediatrics, psychology and psychiatry, and neurology clinics.

This study was approved by the CHOP Institutional Review Board with a waiver of consent.

Study Design and Patient Population

The cohort included all children who presented for a well-child visit (1) between 16 and 26 months of age, (2) at a CHOP site where universal screening had been initiated, and (3) between January 2011 and July 2015 to allow for longitudinal follow-up through ≥4 years. If the child's first screening occurred before initiation of universal screening and the second occurred after universal screening initiation, the first screening was included to accurately represent first and second screens. Screenings at sick visits were also included (0.3% of M-CHAT/F administrations). When multiple M-CHAT/Fs were completed, the first administration was used unless otherwise noted.

Preliminary analyses of screening rates and results included the entire cohort. Children without a primary care visit at ≥4 years of age were excluded from diagnostic outcome analyses because of insufficient length of follow-up. Four years was chosen given recent estimates of the median age of diagnosis for ASD.[18] Those without a documented language of English or Spanish (n = 82; 0.004%) were also excluded because the M-CHAT/F was not available in other languages.

The subgroup whose visits closely followed AAP guidelines was also examined; these children were screened during primary care visits at 18 months (±2) and 24 months (±2) with ≥3 months between screenings.

Measures and EHR Methods

Demographic Data

Demographics, gestational age, and insurance payer for the screening visit were extracted from the EHR. Federal information processing standard codes were linked to census tract–level data to generate estimates of median income, and a median split was performed. Language was coded as English only (ie, only English was documented) or other language (ie, documentation of any non-English language).

Diagnostic Data

Diagnoses were extracted from visit diagnoses and problem lists (a comprehensive list of active and relevant past diagnoses). All available data were used to determine diagnostic outcome. As a result, the length of follow-up period varied across children (although all children included in these analyses had follow-up through at least 4 years).

Children were considered to have ASD if an ASD diagnosis appeared in the EHR more than once or was provided by a specialist because these criteria have been associated with the greatest accuracy in other large health care systems.[19,20] For example, when comparing EHR diagnostic codes and manual chart review, Coleman et al[20] found that ≥2 ASD diagnoses yielded a PPV of 87%; specialist diagnoses were also associated with higher odds of a confirmed diagnosis.

Children were considered to have a non-ASD disorder and/or delay if they did not meet ASD classification criteria described above but had ≥1 code from 1 of the following categories: attention-deficit/hyperactivity disorder (ADHD) and related behaviors, anxiety disorder and related behaviors, disruptive behavior disorder and related behaviors, developmental delay, language disorder and/or delay, motor disorder and/or delay, sensory processing difficulty, and social delay without ASD. See Supplemental Table 5 for specific diagnostic codes used.

Statistical Analyses

Screening rates and results were summarized with percentages; χ^2 analyses and odds ratios (ORs) were calculated for subgroup comparisons. Sensitivity, specificity, PPV, and NPV were calculated from 2 × 2 contingency tables. Effect sizes for the proportion comparisons (Cohen's h) and measures of statistical significance (2-sample tests of proportion) were used to estimate differences in M-CHAT/F accuracy across subgroups. Emphasis was placed on interpreting effect sizes rather than P values alone given the likelihood of statistical significance for trivial differences in this large cohort. Thus, only results with statistically significant comparisons and effect sizes ≥0.20 are reported as meaningful. Finally, Kaplan-Meier survival curves estimated the cumulative probability of ASD diagnosis across time since screening. The log-rank test was used to compare survival curves between children who screened negative and positive to detect differences in mean time to diagnosis by M-CHAT/F outcome.

RESULTS

Screening Rates

A total of 25 999 children had 42 973 eligible visits during the study period (see Table 1 and Fig 1). A total of 23 634 children (90.9%) were screened and 50.4% were screened more than once. White children were screened more often than other racial

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TABLE 1 Cohort Demographics

Entire Cohort	*N* = 25 999
Sex, *n* (%)	
Female	12 553 (48.3)
Male	13 446 (51.7)
Gestational age, *n* (%)	
Full term, 37+ wk	20 249 (77.9)
Premature, <37 wk	2870 (11.0)
Gestational age not documented in the EHR	2880 (11.1)
Language documented in the EHR, *n* (%)	
English only	24 371 (93.7)
Language other than English	1271 (4.9)
No language documented in the EHR	357 (1.4)
Race, *n* (%)	
White	11 118 (42.8)
Black	9497 (36.5)
Asian	1109 (4.3)
Other or multiple races	4232 (16.3)
Race not documented in the EHR	43 (0.2)
Ethnicity, *n* (%)	
Not Hispanic or Latino	23 983 (92.2)
Hispanic or Latino	1929 (7.4)
Ethnicity not documented in the EHR	87 (0.3)
Insurance payer at screening visit	
Private insurance	14 087 (54.2)
Public insurance/Medicaid	11 769 (45.3)
Self-pay or other	143 (0.6)
Type of primary care site at first visit, *n* (%)	
Urban, *n* = 4 sites	10 958 (42.1)
Suburban, *n* = 27 sites	15 041 (57.9)
Median income, $, (SD)[a]	59 596.56 (32 579.09)

[a] Missing for 17 children because the median income was unavailable for the census tract.

groups (see Table 2). Children with English-only exposure, higher incomes, private insurance, and from suburban primary care sites were also screened more often, and premature children were screened less often. Only 47.8% were screened at 18 and 24 months largely because of failure to attend both well-child visits. Children who received 2 screenings according to the AAP schedule were more likely to be white and non-Hispanic, from a suburban site, and have English-only exposure, higher incomes, and private insurance (see Table 2).

Screen-Positive Rates

When considering the first M-CHAT/F, 9.5% (*n* = 2256) screened positive on the 23-item questionnaire, a rate comparable to other large-scale US-based screening studies.[9,21] Of those that screened positive, 88.7% (*n* = 2002) required the follow-up interview (ie, scores of 3–7) and 41.2% (*n* = 825) were administered it. Almost all (*n* = 782; 94.8%) no longer screened positive after the follow-up interview. Of note, these numbers reflect all screened children (including those without follow-up data), so they differ somewhat from Fig 2, which only includes children included in accuracy analyses (ie, screened with follow-up data).

For accuracy analyses, children who screened negative after the questionnaire or follow-up interview were considered screen negatives. Those who continued to screen positive after the interview were considered screen positives. Children who screened positive on the questionnaire but did not receive the follow-up interview were also considered screen positives. Excluding this group would introduce substantial bias to the cohort because there were demographic and clinical differences between children who did and did not receive the follow-up interview (see below). Furthermore, the positive questionnaire results were available to providers to base clinical action on (even in the absence of the follow-up interview), and many were referred after an incomplete M-CHAT/F screening (K.W., W.G., A.B., et al, unpublished data).

This approach resulted in a final screen-positive rate of 6.2%. Children of color, those from lower-income households, with public insurance/

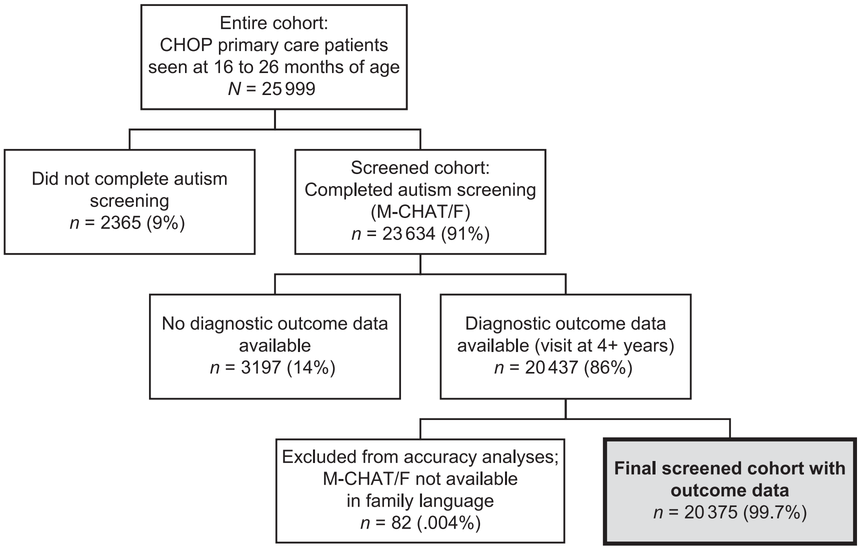
Entire cohort:
CHOP primary care patients
seen at 16 to 26 months of age
N = 25 999
Did not complete autism screening
n = 2365 (9%)
Screened cohort:
Completed autism screening
(M-CHAT/F)
n = 23 634 (91%)
No diagnostic outcome data available
n = 3197 (14%)
Diagnostic outcome data available (visit at 4+ years)
n = 20 437 (86%)
Excluded from accuracy analyses;
M-CHAT/F not available
in family language
n = 82 (.004%)
Final screened cohort with outcome data
n = 20 375 (99.7%)

FIGURE 1
Cohort flowchart.

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TABLE 2 Screening and Follow-up Rates by Child and Family Characteristics

	Screened at Least Once		Screened at 18 and 24 mo		CHOP Patient Through at Least 4 y of Age (ie, Follow-Up Data Available)	
	No. (%)	OR (95% CI)	No. (%)	OR (95% CI)	No. (%)	OR (95% CI)
Entire cohort (*N* = 25 999)	23 628 (90.9)	—	12 418 (47.8)	—	22 392 (86.1)	—
By sex						
Female (*n* = 12 553)	11 375 (90.6)	0.94 (0.86–1.02)	5936 (47.3)	0.96 (0.92–1.01)	10 841 (86.4)	1.04 (0.97–1.11)
Male (*n* = 13 446)	12 253 (91.1)	—	6482 (48.2)	—	11 551 (85.9)	—
By gestational age						
Full term, 37+ wk (*n* = 20 249)	18 567 (91.7)	2.00 (1.79–2.24)[a]	10 051 (49.6)	1.69 (1.56–1.83)[a]	17 658 (87.2)	1.15 (1.03–1.29)[a]
Premature, <37 wk (*n* = 2870)	2429 (84.6)	—	1057 (36.8)	—	2454 (85.5)	—
By language documented in the EHR						
English only (*n* = 24 371)	22 221 (91.2)	2.02 (1.73–2.36)[a]	11 800 (48.4)	1.69 (1.50–1.90)[a]	21 244 (87.2)	1.27 (1.09–1.48)[a]
Language other than English (*n* = 1271)	1063 (83.6)	—	454 (35.7)	—	1071 (84.3)	—
By race						
White (*n* = 11 118)	10 761 (96.8)	—	7151 (64.3)	—	9710 (87.3)	—
Black (*n* = 9497)	7924 (83.4)	5.98 (5.32–6.74)[a]	2637 (27.8)	4.69 (4.42–4.98)[a]	8236 (86.7)	1.05 (0.97–1.15)[a]
Asian (*n* = 1109)	1016 (91.6)	2.76 (2.18–3.50)[a]	566 (51.0)	1.73 (1.53–1.96)[a]	888 (80.1)	1.72 (1.47–2.01)[a]
Other or multiple races (*n* = 4232)	3884 (91.8)	2.70 (2.32–3.14)[a]	2039 (48.2)	1.94 (1.81–2.08)[a]	3527 (83.3)	1.38 (1.25–1.52)[a]
By ethnicity						
Not Hispanic or Latino (*n* = 23 983)	21 811 (90.9)	1.07 (0.92–1.25)	11 544 (48.1)	1.21 (1.10–1.33)[a]	20 724 (86.4)	1.15 (1.01–1.31)[a]
Hispanic or Latino (*n* = 1929)	1743 (90.4)	—	836 (43.3)	—	1633 (84.7)	—
By insurance payer at screening visit						
Private insurance (*n* = 14 087)	13 437 (95.4)	3.45 (3.79–3.13)[a]	8668 (61.5)	3.42 (3.26–3.61)[a]	12 212 (87.1)	1.19 (1.11–1.28)[a]
Public insurance/Medicaid (*n* = 11 769)	10 086 (85.7)	—	3743 (31.8)	—	9955 (85.0)	—
By primary care site type						
Suburban (*n* = 15 041)	14 667 (97.5)	8.77 (7.81–9.80)[a]	2917 (26.6)	4.72 (4.48–5.00)[a]	13 101 (87.1)	1.21 (1.13–1.30)[a]
Urban (*n* = 10 958)	8961 (81.8)	—	9501 (63.2)	—	9291 (84.8)	—
By median income						
Higher income (*n* = 12 991)	12 571 (96.8)	5.26 (4.70–5.86)[a]	4249 (32.7)	3.48 (3.31–3.67)[a]	11 306 (87.0)	1.16 (1.08–1.25)[a]
Lower income (*n* = 12 991)	11 049 (85.1)	—	8167 (62.9)	—	11 074 (85.2)	—

The last group listed is the reference group for ORs, except for comparisons by race. Here, black, Asian, and other or multiple races are the reference groups, respectively, and compared with the white group. Some subgroups do not add to 25 999 participants because of missing data. CI, confidence interval; —, not applicable.

[a] Indicates screening percentages that are different by subgroup at $P < .05$ after Bonferroni correction.

Medicaid and non-English exposure, and those seen in urban practices screened positive more frequently, as did boys and premature children (see Table 2).

Screen-Positive Rates by Age

Older toddlers (21–26 months) screened positive more often (8.9%) than younger toddlers (16–20 months; 5.5%) on the first screening (see Table 3). However, screen-positive rates were somewhat higher at 18 months (4.2%) than at 24 months (3.5%) in the subgroup screened twice; 6.4% screened positive on 1 or both screenings.

Outcome Diagnostic Data

Most screened children (*n* = 20 437; 86.5%) continued to receive CHOP primary care at ≥4 years and were included in M-CHAT/F accuracy analyses because outcome diagnostic data were available. ASD prevalence was 2.2%, which is comparable to recent prevalence estimates in nearby New Jersey.[1,22] A total 62.8% received an ASD diagnosis by a specialist (of these, 94.7% also had an ASD diagnosis documented by a primary care provider); the remaining 37.2% only had a diagnosis made or documented by a primary care provider.

Overall, 36.4% had other delays and/or concerns, which included codes related to development (10.6%), language (23.0%), behavior (8.4%), motor (7.9%), ADHD and related behaviors (2.9%), anxiety and related behaviors (1.8%), sensory processing (0.4%), and social delays without ASD (0.6%; categories are not mutually exclusive).

Accuracy Analyses

The M-CHAT/F's sensitivity to detect ASD was 38.8%, and its specificity was 94.9%. PPV was 14.6% and NPV was 98.6% (see Table 4, Fig 2, and Fig 3). The M-CHAT/F's accuracy in detecting any documented delay and/or concern (including ASD) was as follows: sensitivity was 11.8%, specificity was 97.4%, PPV was 72.4%, and NPV was 65.9%.

Effect of Age and Multiple Screenings

Across all first-time screenings, screenings at older ages (21–26 months) were more sensitive than at younger ages (16–20 months; 48.8% vs 35.1%). In the AAP subgroup of children screened twice, the second screening at 24 months was marginally more sensitive (39.8% vs 31.8%) and had higher PPV (24.7%

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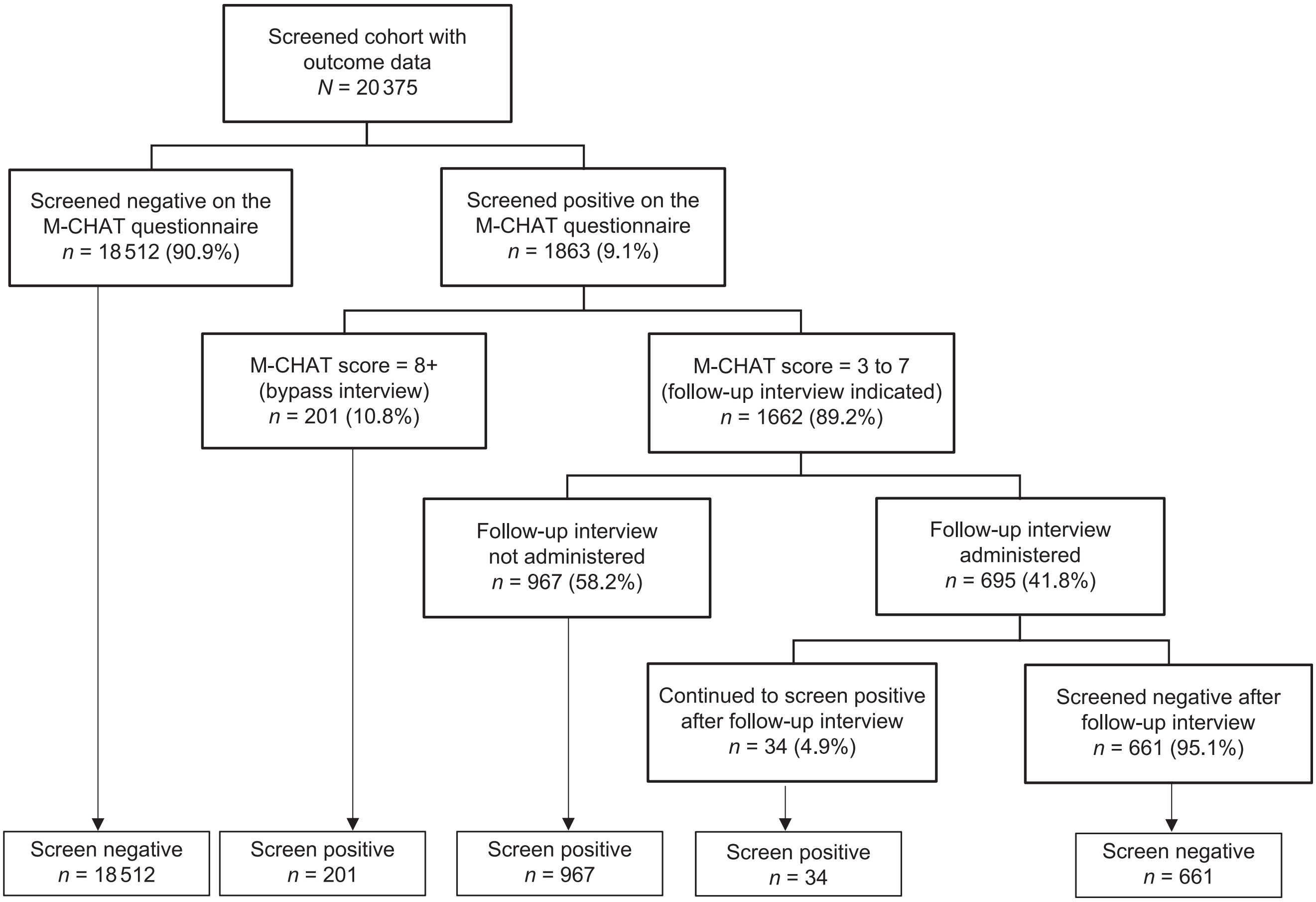
Screened cohort with outcome data
N = 20 375
Screened negative on the M-CHAT questionnaire
n = 18 512 (90.9%)
Screened positive on the M-CHAT questionnaire
n = 1863 (9.1%)
M-CHAT score = 8+ (bypass interview)
n = 201 (10.8%)
M-CHAT score = 3 to 7 (follow-up interview indicated)
n = 1662 (89.2%)
Follow-up interview not administered
n = 967 (58.2%)
Follow-up interview administered
n = 695 (41.8%)
Continued to screen positive after follow-up interview
n = 34 (4.9%)
Screened negative after follow-up interview
n = 661 (95.1%)
Screen negative
n = 18 512
Screen positive
n = 201
Screen positive
n = 967
Screen positive
n = 34
Screen negative
n = 661

FIGURE 2
M-CHAT/F results for screened cohort with outcome data.

vs 16.4%) than the first screening at 18 months. Combining results from 18- and 24-month screenings yielded greater sensitivity than either screening alone (51.1%). See Table 4.

Effect of Child and/or Family Characteristics

Despite comparable sensitivities across racial groups, specificity and PPV were higher in white children (97.9%; 24.0%) compared with black children (91.7%; 11.7%), Asian children (90.4%; 10.8%), and those from other or multiple racial groups (93.8%; 13.4%). Differences were not observed between black, Asian, and other or multiple racial groups, or by ethnicity.

Higher specificity and PPV were observed in children with English-only exposure compared with children with non-English exposure (95.2% vs 86.9%; 15.3% vs 8.5%) as well as children from higher- versus lower-income families (97.0% vs 92.3%; 20.4% vs 11.8%). The same pattern was observed for insurance payer because children with private insurance had higher specificity (97.6% vs 91.0%) and PPV (22.1% vs 11.3%). This pattern was also observed for practice type because specificity was higher in children screened in suburban sites (96.8% vs 91.5%) as was PPV, although this effect size fell below the cutoff (h = 0.18; 18.5% vs 12.0%).

PPV was higher in boys than in girls (19.9% vs 7.7%). Sensitivity was higher in children born premature (54.3% vs 35.8%), but specificity was lower (89.3% vs 95.4%).

Effect of Follow-up Interview Administration

Children requiring the follow-up interview (ie, scores of 3–7) who received it were more likely to be full term (P = .007; OR = 1.41), have lower incomes ($P < .001$; OR = 1.65), and be from urban practices ($P < .001$; OR = 1.60) than those who did not receive the follow-up interview. Black children were also more likely than white (P = .001; OR = 1.48), Asian (P = .06; OR = 1.40), or children of other or multiple races ($P < .001$; OR = 1.64) to receive the follow-up interview. Children without ASD were also more likely to receive the follow-up interview than children with ASD (P = .02; OR = 1.54).

PPV was examined separately on the basis of the presence or absence of follow-up interview results. PPV was

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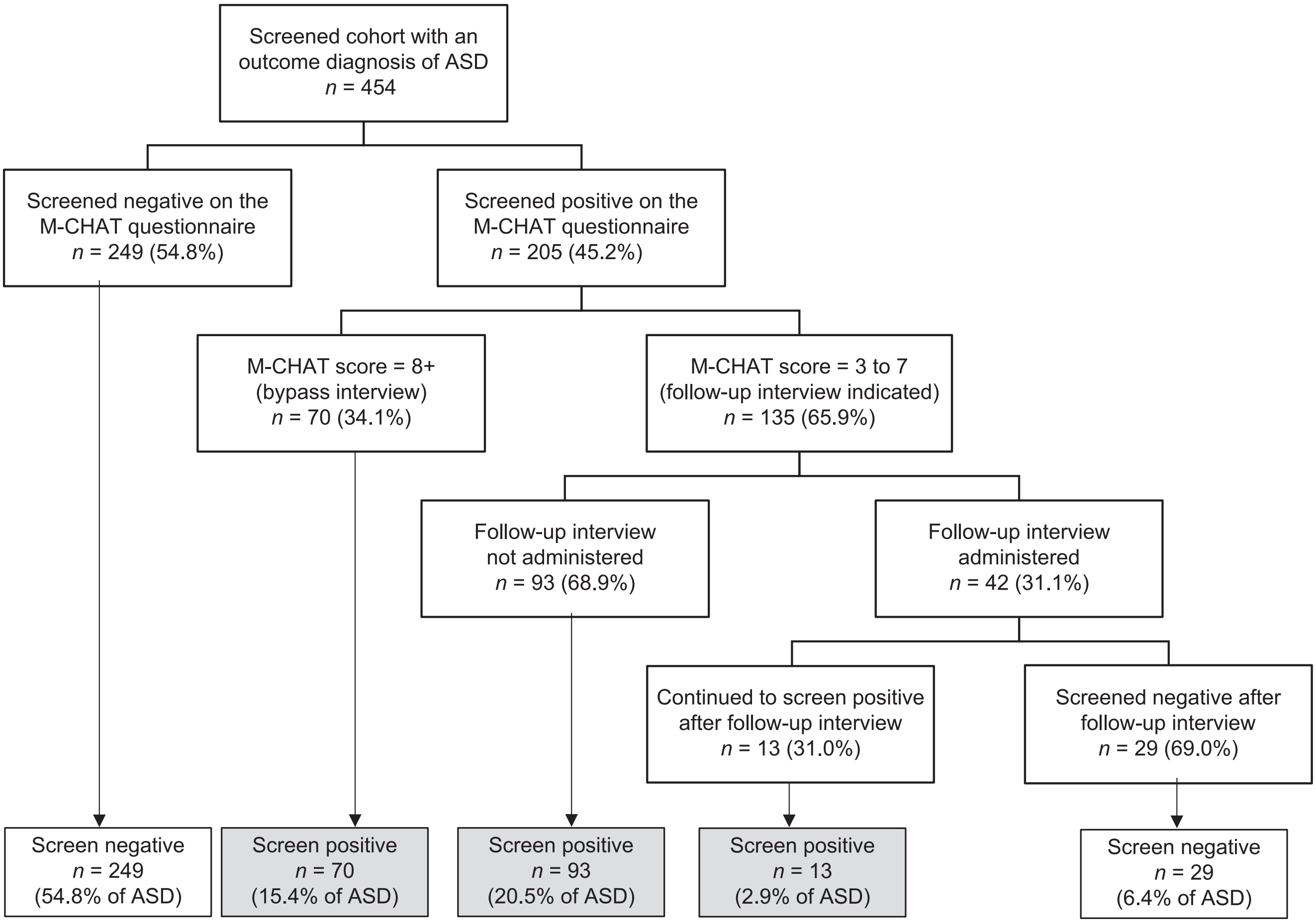

FIGURE 3
M-CHAT/F results for screened cohort with outcome diagnosis of ASD.

34.8% in children with a questionnaire score of 8+ (ie, follow-up interview bypassed, *n* = 201). PPV was 38.2% in children who continued to screen positive after receiving the follow-up interview (*n* = 34). PPV was 9.6% in those that did not receive the interview (*n* = 967). Other metrics could not be calculated separately by follow-up results because they are calculated by using screen negatives, and it is not possible to know how many of the 967 children who did not receive the interview would have screened negative.

Excluding all follow-up interview data (ie, M-CHAT/F questionnaire results), sensitivity was 45.2%, specificity was 91.7%, PPV was 11.0%, and NPV was 98.7%.

M-CHAT/F Results and Time to Diagnosis

Kaplan-Meier survival curves revealed that the mean time to diagnosis was significantly shorter for children with ASD who screened positive than for those who screened negative (mean difference = 7.45 months; $P < .001$).

DISCUSSION

In this study we examined the M-CHAT/F's accuracy within a universally screened cohort. The results revealed high screening rates, achieved through robust EHR support for screening. Systematic follow-up of children who screened positive and negative allowed an estimation of sensitivity, specificity, PPV, and NPV. The M-CHAT/F's sensitivity to detect ASD was just 39%, indicating that the majority of children later diagnosed with ASD screened negative. PPV was just 15%, an estimate consistent with recent large (but not universally screened) studies conducted in Norway and Malaysia.[14,15] However, this estimate was much lower than that found in some US-based studies conducted in research settings, likely partially because of different prevalence rates across studies.[9,21] PPV improved substantially when any diagnosis or concern was considered (72%). Specificity and NPV for ASD were high (95% and 99%, respectively), but it is important to remember that with low prevalence and screen-positive rates, specificity and NPV will tend toward high rates.

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TABLE 3 M-CHAT/F Screen-Positive Rates by Child and Family Characteristics

	Screened Positive on M-CHAT/F, No. (%)	OR (95% CI)
Screened cohort (*n* = 23 628)	1474 (6.2)	—
By age at first screening		
16–20 mo (*n* = 18 585)	1027 (5.5)	—
21–26 mo (*n* = 5043)	447 (8.9)	1.66 (1.48–1.87)[a]
By multiple screenings		
First screening at ~18 mo (*n* = 11 624)	518 (4.2)	—
Second screening at ~24 mo (*n* = 11 624)	440 (3.5)	0.84 (0.74–0.96)[a]
By sex		
Female (*n* = 11 375)	635 (5.6)	—
Male (*n* = 12 253)	839 (6.8)	1.24 (1.12–1.38)[a]
By gestational age		
Full term, 37+ wk (*n* = 18 567)	1022 (5.5)	—
Premature, <37 wk (*n* = 2429)	302 (12.4)	2.44 (2.13–2.80)[a]
By language documented in the EHR		
English only (*n* = 22 221)	1301 (5.9)	—
Language other than English (*n* = 1063)	159 (15.0)	2.83 (2.37–3.38)[a]
By race		
White (*n* = 10 761)	319 (3.0)	—
Black (*n* = 7924)	752 (9.5)	3.45 (3.01–3.94)[a]
Asian (*n* = 1016)	108 (10.6)	3.90 (3.11–4.90)[a]
Other or multiple races (*n* = 3884)	295 (7.6)[c]	2.70 (2.29–3.16)[a]
By ethnicity		
Not Hispanic or Latino (*n* = 21 811)	1305 (6.0)	—
Hispanic or Latino (*n* = 1743)	167 (9.6)	1.67 (1.41–1.97)[a]
By insurance payer at screening visit		
Private insurance (*n* = 13 437)	427 (3.2)	—
Public insurance/Medicaid (*n* = 10 086)	1038 (10.3)	3.50 (3.11–3.93)[a]
By primary care site type		
Suburban (*n* = 14 667)	610 (4.2)	—
Urban (*n* = 8961)	864 (9.6)	2.46 (2.21–2.74)[a]
By median income		
Higher income (*n* = 12 571)	496 (3.9)	—
Lower income (*n* = 11 049)	977 (8.8)	2.36 (2.11–2.64)[a]

The first group listed is the reference group for ORs. Some subgroups do not add to 23 628 participants because of missing data. A comparison of the first and second screening was conducted in subsample with 2 screenings according to AAP guidelines (*n* = 11 624 children). CI, confidence interval; —, not applicable.

[a] Indicates screen-positive rates that are different by subgroup at $P < .05$ after Bonferroni correction.

Although the M-CHAT/F identified fewer children with ASD than expected, those who did screen positive received an ASD diagnosis 7 months earlier than those who screened negative. This suggests that a positive M-CHAT/F screening may have contributed to an earlier diagnosis for children with ASD in this cohort. However, continued research is needed to understand the specific effect of a positive screen on age of diagnosis.

The M-CHAT/F was significantly more sensitive at older ages (49% at 21–26 months) than at younger ages (35% at 16–20 months). However, PPV did not improve with age (16% vs 14%), which is in contrast to findings from some previous studies.[12] PPV did improve for repeated screenings; 25% of children who screened positive at the second screening had ASD (regardless of results of the first screening) compared with 17% for the first screen. These results highlight the potential importance of screening twice as well as the difficulty of accurate screening at ~18 months.

Sensitivity was higher, but specificity was lower for premature children compared with those born full term, consistent with several other studies in very premature children.[23–25] PPV was lower in girls (8%) than in boys (20%), but it is unclear whether this was because of delayed diagnosis for some girls or poorer M-CHAT/F performance in girls, but future research should be used to examine sex differences in each stage of detection, from screening to diagnosis.

Although electronic screening yielded high screening rates, when children were missed, they were more likely to be children of color, from lower-income households, seen in an urban practice, receive public insurance/Medicaid, and be exposed to a language other than English. These same children were also less likely to present for 2 well-child visits, resulting in disparities in receiving care according to AAP guidelines.

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TABLE 4 M-CHAT/F Accuracy in Detecting ASD by Child and Family Characteristics

	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Screened cohort with outcome data (n = 20 375)	38.8 (34.3–43.3)	94.9 (94.5–95.2)	14.6 (12.6–16.6)	98.6 (98.4–98.7)
By age at first screening				
16–20 mo	35.1 (30.0–40.3)[a]	95.4 (95.1–95.7)	13.9 (11.6–16.2)	98.6 (98.4–98.8)
21–26 mo	48.8 (39.6–57.7)[a]	92.3 (92.0–93.5)	16.4 (12.6–20.3)	98.4 (98.0–98.8)
Comparison of accuracy by age	$P = .009$, $h = 0.28$[a]	$P < .001$, $h = 0.11$	$P = .25$, $h = 0.07$	$P = .41$, $h = 0.01$
By multiple screenings				
First screening only at ~18 mo without regard for results of second screening	31.8 (25.9–37.7)[a]	96.6 (96.3–97.0)	17.0 (13.5–20.4)	98.5 (98.3–98.7)
Second screening only at ~24 mo without regard for results of second screening	39.8 (33.5–46.0)	97.4 (97.1–97.7)	24.7 (20.4–29.1)	98.7 (98.5–98.9)
Comparison of accuracy by screening, first vs second	$P = .07$, $h = 0.17$	$P = .001$, $h = 0.04$	$P = .006$, $h = 0.19$	$P = .25$, $h = 0.02$
First or second screening positive	51.1 (44.7–57.4)[a]	94.8 (94.4–95.2)	17.6 (14.8–20.5)	98.9 (98.7–99.1)
Comparison of accuracy by no. of screenings, first screening vs both screenings	$P < .001$, $h = 0.39$[a]	$P < .001$, $h = 0.09$	$P = .77$, $h = 0.02$	$P = .01$, $h = 0.04$
By sex				
Female	39.6 (30.1–49.1)	95.1 (94.7–95.5)	7.7 (5.4–10.0)[a]	99.4 (99.2–99.5)
Male	38.5 (33.5–43.6)	94.6 (94.2–95.1)	19.9 (16.9–22.9)[a]	97.8 (97.5–98.1)
Comparison of accuracy by sex	$P = .85$, $h = 0.02$	$P = .15$, $h = 0.02$	$P < .001$, $h = 0.36$[a]	$P < .001$, $h = 0.14$
By gestational age				
Full term, 37+ wk	35.8 (30.8–40.8)[a]	95.4 (95.1–95.8)[a]	14.8 (12.4–17.2)	98.6 (98.4–98.7)
Premature, <37 wk	54.3 (42.6–66.0)[a]	89.3 (87.9–90.6)[a]	15.0 (10.6–19.4)	98.2 (97.6–98.8)
Comparison of accuracy by gestational age	$P = .004$, $h = 0.37$[a]	$P < .001$, $h = 0.24$[a]	$P = .90$, $h = 0.01$	$P = .31$, $h = 0.02$
By language documented in the EHR				
English only	38.5 (33.9–43.1)	95.2 (94.9–95.5)[a]	15.3 (13.2–17.5)[a]	98.6 (98.4–98.7)
Language other than English	43.5 (23.2–63.7)	86.9 (84.6–89.2)[a]	8.5 (3.4–13.5)[a]	98.2 (97.3–99.2)
Comparison of accuracy by language	$P = .63$, $h = 0.10$	$P < .001$, $h = 0.30$[a]	$P = .046$, $h = 0.21$[a]	$P = .46$, $h = 0.03$
By race				
White	37.7 (30.4–45.1)	97.9 (97.6–98.1)[a]	24.0 (18.9–29.2)[a]	98.9 (98.6–99.1)
Black	40.7 (33.5–47.8)	91.7 (91.0–92.3)[a]	11.7 (9.2–14.2)[a]	98.3 (98.0–98.6)
Comparison of accuracy by race vs white	$P = .58$, $h = 0.06$	$P < .001$, $h = 0.29$[a]	$P < .001$, $h = 0.33$[a]	$P = .002$, $h = 0.05$
Asian	30.0 (13.6–46.4)	90.4 (88.3–92.4)[a]	10.8 (4.2–17.5)[a]	97.1 (95.8–98.3)
Comparison of accuracy by race vs white	$P = .42$, $h = 0.16$	$P < .001$, $h = 0.34$[a]	$P = .01$, $h = 0.35$[a]	$P < .001$, $h = 0.13$
Other or multiple races	40.0 (28.9–51.1)	93.8 (93.0–94.7)[a]	13.4 (8.9–17.9)[a]	98.5 (98.1–98.9)
Comparison of accuracy by race vs white	$P = .73$, $h = 0.05$	$P < .001$, $h = 0.21$[a]	$P = .003$, $h = 0.28$[a]	$P = .11$, $h = 0.03$
By ethnicity				
Hispanic or Latino	42.1 (26.4–57.8)	92.2 (90.8–93.6)	12.5 (6.8–18.2)	98.4 (97.7–99.0)
Not Hispanic or Latino	38.5 (33.8–43.1)	95.1 (94.7–95.4)	14.9 (12.8–17.0)	98.6 (98.4–98.7)
Comparison of accuracy by ethnicity	$P = .66$, $h = 0.07$	$P < .001$, $h = 0.12$	$P = .47$, $h = 0.07$	$P = .56$, $h = 0.02$
By insurance payer at screening visit				
Public insurance/Medicaid	42.8 (36.3–49.3)	91.0 (90.4–91.6)[a]	11.3 (9.1–13.4)[a]	98.3 (98.1–98.6)
Private insurance	34.4 (28.2–40.5)	97.6 (97.3–97.9)[a]	22.1 (17.8–26.4)[a]	98.7 (98.5–98.9)
Comparison of accuracy by insurance	$P = .07$, $h = 0.17$	$P < .001$, $h = 0.30$[a]	$P < .001$ $h = 0.29$[a]	$P = .05$, $h = 0.03$
By primary care site type				
Urban	40.2 (33.6–46.8)	91.5 (90.9–92.1)[a]	12.0 (9.6–14.4)	98.1 (97.8–98.5)
Suburban	37.5 (31.4–43.6)	96.8 (96.5–97.1)[a]	18.5 (15.0–21.9)	98.8 (98.6–99.0)
Comparison of accuracy by site type	$P = .56$, $h = 0.06$	$P < .001$, $h = 0.23$[a]	$P = .002$, $h = 0.18$	$P < .001$, $h = 0.05$
By median income				
Lower income	39.0 (32.8–45.2)	92.3 (91.8–92.9)[a]	11.8 (9.5–14.0)[a]	98.3 (98.0–98.6)
Higher income	38.7 (32.1–45.2)	97.0 (96.7–97.3)[a]	20.4 (16.5–24.4)[a]	98.8 (98.6–99.0)
Comparison of accuracy by income	$P = .94$, $h = 0.01$	$P < .001$, $h = 0.22$[a]	$P < .001$, $h = 0.24$[a]	$P = .006$, $h = 0.04$

CI, confidence interval.

[a] These comparisons are statistically significant ($P < .05$) and clinically meaningful ($h \geq 0.20$).

Despite these disparities, screening rates among children from traditionally underrepresented groups were still relatively high (>80%). Children of color and those from lower-income households screened positive at 2 to 3 times the rates of white, higher-income, privately insured, and suburban children. Elevated screen-positive rates resulted in somewhat higher sensitivity to detect ASD but also higher false-positive rates (ie, lower PPV and specificity) in these groups. It is suggested by these data that disparities in age of diagnosis are likely preceded by disparities in screening rates and differential accuracy of screening tools for children from underrepresented and underresourced groups. Future

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research should attempt to disentangle the effects of race and/or ethnicity, income, language, and primary care setting to better understand the role of child-, family-, and practice-level variables on screening.

With regard to the follow-up interview, pediatricians did not complete the interview systematically but instead may have used clinical judgement when deciding when to administer. Children who received the follow-up interview were significantly less likely to have ASD, and when children received the follow-up, almost all (95%) screened negative. Thus, pediatricians may have used the interview to confirm a clinical opinion of "not ASD" and chosen to skip the interview and go straight to referral when they suspected ASD. Additional research is needed to disentangle differences in follow-up interview rates by race and income; this may have been a clinical adaptation to artificially high screen-positive rates or it may incorrectly delay diagnosis for these children. However, the follow-up interview did appear to reduce false-negatives (ie, improve PPV), underscoring the importance of this step of the screening process.

There are limitations to the current study, largely surrounding the real-world nature of this cohort. Although this epidemiological study represented all children within the CHOP primary care network, findings may not generalize to other populations, particularly those with less access to ASD specialty care. Diagnoses were given in real-world clinical settings rather than through rigorous research studies. Diagnostic information was also only available through 4 to 8 years of age, so the M-CHAT/F's accuracy may differ as children in this cohort age.

The M-CHAT/F, rather than the M-CHAT–R/F, was used, although accuracy of these 2 versions is comparable.[9] As indicated above, not all eligible children received the follow-up interview, which likely downwardly biased specificity and PPV and upwardly biased sensitivity and NPV in that some would have screened negative if they had received the follow-up interview. Thus, this study cannot estimate the accuracy of perfect M-CHAT/F administration but instead provides critical information on how well this tool detects ASD in a real-world, universally screened cohort.

CONCLUSIONS

These results suggest that universal screening in primary care is possible when supported by electronic administration and EHR integration. However, universal screening and systematic follow-up revealed low accuracy of the M-CHAT/F, particularly for children of color and those from lower-income households. Although some may interpret these findings as evidence against universal screening, we caution against this interpretation given the earlier age of diagnosis for screen positives. Instead, results suggest that augmentative screening methods should be developed to detect more children through universal screening efforts and reduce disparities. Promising new methods include parent-report tools that are supported by picture or video models[26] and direct data gathering methods that leverage technological advances in computing and machine learning.[27,28] However, any new method should be tested in cohorts that are universally screened and systematically followed-up to reduce the bias associated with screening and following selected populations.

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ABBREVIATIONS

AAP: American Academy of Pediatrics
ADHD: attention-deficit/hyperactivity disorder
ASD: autism spectrum disorder
CHOP: Children's Hospital of Philadelphia
EHR: electronic health record
M-CHAT: Modified Checklist for Autism in Toddlers without Follow-Up
M-CHAT/F: Modified Checklist for Autism in Toddlers with Follow-Up
M-CHAT–R/F: Modified Checklist for Autism in Toddlers, Revised, with Follow-Up
NPV: negative predictive value
OR: odds ratio
PPV: positive predictive value

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Accuracy of Autism Screening in a Large Pediatric Network

Whitney Guthrie, Kate Wallis, Amanda Bennett, Elizabeth Brooks, Jesse Dudley,
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Trends in Psychiatric Emergency Department Visits Among Youth and Young Adults in the US

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abstract

BACKGROUND: Visits to the emergency department (ED) for psychiatric purposes are an indicator of chronic and acute unmet mental health needs. In the current study, we examined if psychiatric ED visits among individuals 6 to 24 years of age are increasing nationwide.

METHODS: ED data came from the 2011–2015 National Hospital Ambulatory Medical Care Survey, a national survey of ED visits across the United States. Psychiatric ED visits were identified by using the *International Classification of Diseases, Ninth Revision* and reason-for-visit codes. Survey-weighted logistic regression analyses were employed to examine trends in as well as correlates of psychiatric ED visits. Data from the US Census Bureau were used to examine population rates.

RESULTS: Between 2011 and 2015, there was a 28% overall increase (from 31.3 to 40.2) in psychiatric ED visits per 1000 youth in the United States. The largest increases in psychiatric ED visits per 1000 US youth were observed among adolescents (54%) and African American (53%) and Hispanic patients (91%). A large increase in suicide-related visits (by 2.5-fold) was observed among adolescents (4.6–11.7 visits per 1000 US youth). Although psychiatric ED visits were long (51% were ≥3 hours in length), few (16%) patients were seen by a mental health professional during their visit.

CONCLUSIONS: Visits to the ED for psychiatric purposes among youth are rising across the United States. Psychiatric expertise and effective mental health treatment options, particular those used to address the rising suicide epidemic among adolescents, are needed in the ED.

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Dr Kalb designed the study, drafted the initial manuscript, and conducted the analyses on the publicly available data set; Drs Stapp, Ballard, Keefer, and Riley and Ms Holingue reviewed and revised the manuscript and provided important intellectual content, including conceptualization of the study design, fit of the current study within the literature, and approach to the analyses; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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WHAT'S KNOWN ON THIS SUBJECT: The emergency department (ED) is the national safety net for individuals with chronic and acute mental health issues. Monitoring trends in ED visits is critical because they can signal important changes in population health.

WHAT THIS STUDY ADDS: Between 2011 and 2015, psychiatric ED visits among youth in the United States increased. This trend was largely driven by adolescents, and youth of color. An increase in visits related to self-injury and suicide was observed among adolescents.

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TABLE 1 Age-Related Characteristics of Psychiatric ED Visits Among Youth in the United States

	6–11 y	12–17 y	18–24 y	Overall
Count of total visits (weighted)	35 497 171	39 393 222	81 201 713	156 092 106
Count of psychiatric ED visits (weighted)	825 616	3 881 608	8 434 362	13 141 586
Estimated youth in the United States, 2011–2015	123 138 640	125 212 948	154 601 355	402 952 943
Psychiatric ED visits, % of all visits (count)				
2011	2.0 (133 225)	9.0 (727 111)	9.4 (1 655 670)	7.8 (2 516 006)
2012	2.0 (132 235)	8.2 (607 112)	9.7 (1 575 440)	7.6 (2 314 787)
2013	2.8 (179 852)	9.4 (675 333)	9.8 (1 507 892)	8.1 (2 363 077)
2014	2.3 (181 471)	9.1 (755 863)	10.7 (1 770 647)	8.3 (2 707 981)
2015	2.5 (198 833)	13.2 (1 116 189)	12.5 (1 924 713)	10.1 (3 239 735)
Psychiatric ED visits per 1000 US youth				
2011	5.4	28.9	54.0	31.3
2012	5.4	24.2	50.9	28.7
2013	7.3	27.0	48.5	29.3
2014	7.3	30.2	57.0	33.5
2015	8.0	44.6	62.5	40.2
Region, % of psychiatric ED visits				
Northeast	29.6	20.6	18.8	20.0
Midwest	22.4	25.9	24.7	25.0
South	29.3	33.9	33.7	33.5
West	18.7	19.5	22.7	21.5
Sex,* %				
Female	28.4	56.7	49.7	50.0
Male	71.6	43.3	50.8	50.0
Race, %				
Non-Hispanic White	55.7	58.6	64.3	62.1
Non-Hispanic African American	22.9	19.4	19.7	19.8
Hispanic	16.5	19.8	13.8	15.8
Non-Hispanic other	4.9	2.1	2.1	2.3
Insurance,* %				
Private	32.2	38.6	32.5	34.3
Public	56.4	52.7	38.0	43.6
Self-pay	6.7	5.9	21.2	15.9
Other	4.6	2.8	8.3	6.4
Visit on a weekend,* %				
No	83.5	76.7	71.9	74.0
Yes	16.5	23.3	28.1	26.0
Arrival time,* %				
Morning (<11 AM)	18.6	20.1	32.7	28.1
Afternoon (11 AM–4 PM)	28.3	31.7	29.2	29.9
Evening (5 PM–12 AM)	53.0	48.2	38.0	42.0
Urgent,* %				
No	34.3	21.9	33.5	30.1
Yes	65.7	78.1	66.5	69.9
Arrive by ambulance,*%				
No	85.9	78.7	71.2	25.6
Yes	14.1	21.3	28.8	74.4
Length of visit, %				
<90 min	18.5	17.4	21.9	20.4
90–179 min	25.7	28.3	28.9	28.5
180–359 min	36.9	30.5	28.3	29.4
≥6 h	18.8	23.7	21.1	21.7
Mental health provider seen,* %				
No	84.5	75.1	87.4	83.5
Yes	15.4	24.9	12.6	16.5
Admit to hospital,* %				

It is estimated that >1 in 10 youth in the United States has a serious psychiatric disorder.[1] Many of these children, however, never receive treatment.[2] For those in crisis (eg, suicide ideation, aggression, and psychosis) or without accessible connections to the mental health care system, the emergency department (ED) has become the national safety net because this setting is obligated to treat all patients regardless of day or time, reason for referral, or availability of financial payment. This status as a frontline provider has led EDs to the breaking point, in which EDs are overcrowded and shutting their doors because of lack of financial protections.[3]

Because the ED is designed as an urgent medical facility, this setting often lacks the resources required to identify and manage psychiatric populations.[4,5] Discharge planning is also a challenge because the wait for outpatient psychiatry is long, and inpatient psychiatric beds are a dwindling resource.[6–8] As a result, ED mental health visits are associated with long wait times, which are due in part to psychiatric "boarding" (in which a patient waits in the ED for an inpatient bed).[9,10]

Pediatric ED visits have steadily increased over the last several decades.[11–16] The most recent estimates suggest that 5% to 7% of all pediatric ED visits in the United States are related to mental health and/or substance abuse.[12,16] This is likely an underestimate because passive mental health reporting, in which providers do not actively screen patients for mental health issues, is the routine procedure in the ED.[4,17] The increased presence of pediatric psychiatric visits in the ED has become such a public health problem that it prompted a 2016 joint statement by the American Academy of Pediatrics and the American College of Emergency Physicians.[4,18]

TABLE 1 Continued

	6–11 y	12–17 y	18–24 y	Overall
No	81.6	74.6	84.3	81.3
Yes or transfer to another hospital	6.3	8.9	9.2	8.9
Transfer or admit to a psychiatric facility	12.1	16.4	6.5	9.8
Any psychiatric diagnosis or RFV,[*,a] %				
Mood[*]	45.4	62.7	48.5	52.5
Behavior[*]	42.3	19.7	8.2	13.7
SUD[*]	4.5	26.6	50.7	40.6
Psychosis	6.2	5.1	7.3	6.6
Suicide attempt or self-injury[*]	4.2	22.7	8.9	12.7
Other[*]	40.8	39.7	24.8	30.2
Count of psychiatric diagnoses or RFVs, mean	1.39	1.53	1.39	1.42
Primary diagnosis is psychiatric,[*] %				
No	37.9	23.3	38.9	34.2
Yes	62.1	76.7	61.1	65.8

[a] Reflects the presence of any of the listed diagnoses or RFVs.

[*] $P < .05$.

In that report, the authors provide clinical recommendations regarding best practices when managing youth with mental health issues in the ED.[4,18]

Less is known about psychiatric ED use among transition-aged adults. Most research has been focused on youth (<17 years of age) or adults (≥18 years), lumping young adults (18–24 years) with older populations who have substantially different mental health profiles.[19,20] Investigating psychiatric ED use among young adults is critical because many serious psychiatric disorders emerge in young adulthood, and both mental health and substance abuse–related problems are directly related to the top 3 leading causes of death for young adults (ie, injury, suicide, and homicide).[21,22]

TABLE 2 Multivariate Analysis of Correlates of Psychiatric ED Visits Among Age Groups

	Children		Adolescents	
	RRR	95% CI	RRR	95% CI
Year	1.04	0.89 to 1.22	1.04	0.94 to 1.14
Region				
Northeast	Reference	Reference	Reference	Reference
Midwest	0.56	0.29 to 1.09	0.99	0.67 to 1.45
South	0.67	0.37 to 1.23	1.04	0.69 to 1.59
West	0.49[*]	0.27 to 0.90	0.74	0.49 to 1.12
Sex				
Female	Reference	Reference	Reference	Reference
Male	2.65[*]	1.67 to 4.19	0.78	0.61 to 0.99
Race and/or ethnicity				
White, non-Hispanic	Reference	Reference	Reference	Reference
African American, non-Hispanic	1.28	0.81 to 2.03	1.10	0.79 to 1.55
Hispanic	1.27	0.64 to 2.52	1.74[*]	1.22 to 2.47
Other	2.96	0.63 to 13.95	1.21	0.54 to 2.74
Insurance				
Private	Reference	Reference	Reference	Reference
Public	1.42	0.79 to 2.57	1.03	0.74 to 1.43
Self-pay	0.30[*]	0.10 to 0.92	0.22[*]	0.14 to 0.34
Other	0.48	0.14 to 1.70	0.26[*]	0.12 to 0.54
Visit on a weekend				
No	Reference	Reference	Reference	Reference
Yes	0.57[*]	0.15 to 0.94	0.86	0.63 to 1.18
Arrival time				
Morning (<11 AM)	Reference	Reference	Reference	Reference
Afternoon (11 AM–4 PM)	1.74	0.91 to 3.14	1.69[*]	1.19 to 2.39
Evening (5 PM–12 AM)	2.35[*]	1.34 to 4.12	2.04[*]	1.49 to 2.80
Urgent				
No	Reference	Reference	Reference	Reference
Yes	0.85	0.50 to 1.44	1.76[*]	1.24 to 2.50
Length of visit	0.99	0.99 to 1.00	1.00	0.99 to 1.00

Understanding psychiatric ED use among youth and young adults is important because the ED is an entryway to the mental health system for many children and families.[23] These visits present a unique opportunity to recognize and initiate treatment services for previously unidentified mental health problems.[4] The ED is also at the front lines of the nation's substance abuse and suicide epidemics, which uniquely situates them to intervene in these public health crises.[24,25]

For the current study, we have 3 aims. First, we provide updated estimates on changes in psychiatric ED visits in the United States (between 2011 and 2015) among youth 6 to 24 years of age. Second, we assessed if there were disparate trends in psychiatric ED visits over time across different age, sex, and racial and/or ethnic groups. Third, we examined correlates of psychiatric ED visits across the different age, sex, and racial and/or ethnic groups. Particular attention was paid to suicidal-attempt and self-injury visits.

METHODS

Data for this study primarily came from the 2011–2015 National Hospital Ambulatory Medical Care Survey (NHAMCS).[26] The NHAMCS is a cross-sectional national probability survey of ED visits across the United States. Survey sampling weights allow for generalization of NHAMCS estimates to all nonfederal, short-stay, and general hospital EDs across the

TABLE 2 Continued

	Children		Adolescents	
	RRR	95% CI	RRR	95% CI
Arrive by ambulance				
No	Reference	Reference	Reference	Reference
Yes	0.39*	0.21 to 0.75	0.71*	0.54 to 0.93
Mental health provider seen				
No	Reference	Reference	Reference	Reference
Yes	1.06	0.32 to 2.11	2.08*	1.46 to 2.96
Admit to hospital				
No	Reference	Reference	Reference	Reference
Yes or transfer to another hospital	0.58	0.31 to 1.11	1.06	0.67 to 1.69
Transfer or admit to a psychiatric facility	1.48	0.61 to 3.58	2.47*	1.49 to 4.11
Psychiatric diagnosis or RFV[a]				
Mood	0.83	0.50 to 1.37	1.57*	1.18 to 2.08
Behavior	7.64*	4.62 to 12.62	2.53*	1.79 to 3.56
SUDs	0.05*	0.02 to 0.13	0.41*	0.30 to 0.54
Psychosis	0.57	0.22 to 1.47	0.67	0.44 to 1.02
Suicide attempt or intentional self-injury	0.47	0.19 to 1.14	3.19*	2.27 to 4.48
Other	1.68*	1.12 to 2.53	1.87*	1.43 to 2.43
Count of diagnoses and/or RFVs	0.86	0.61 to 1.20	1.30*	1.09 to 1.54
Primary diagnosis is psychiatric				
No	Reference	Reference	Reference	Reference
Yes	0.96	0.61 to 1.51	2.21*	1.66 to 2.93

RRR, relative risk ratio.

[a] Reflects the presence of any of the listed diagnoses or RFVs; young adults served as the reference group.

* $P < .05$.

United States. The weights also account for nonresponse by EDs (those that did not participate in the NHAMCS survey), which averaged 11.9% over the 5-study year period.[27]

Data for the NHAMCS are collected during a randomly selected 4-week period of the year. Information from patient medical records is abstracted by trained staff members who use standardized forms. All NHAMCS data are deidentified and publicly available, which allows for this study to be exempt from the local institutional review board. Beyond the NHAMCS, the only other data used in this study were retrieved from the US Census Bureau.[28] Census data (from 2011 to 2015) were used for calculating population-based rates of psychiatric ED visits per 1000 youth in the United States.

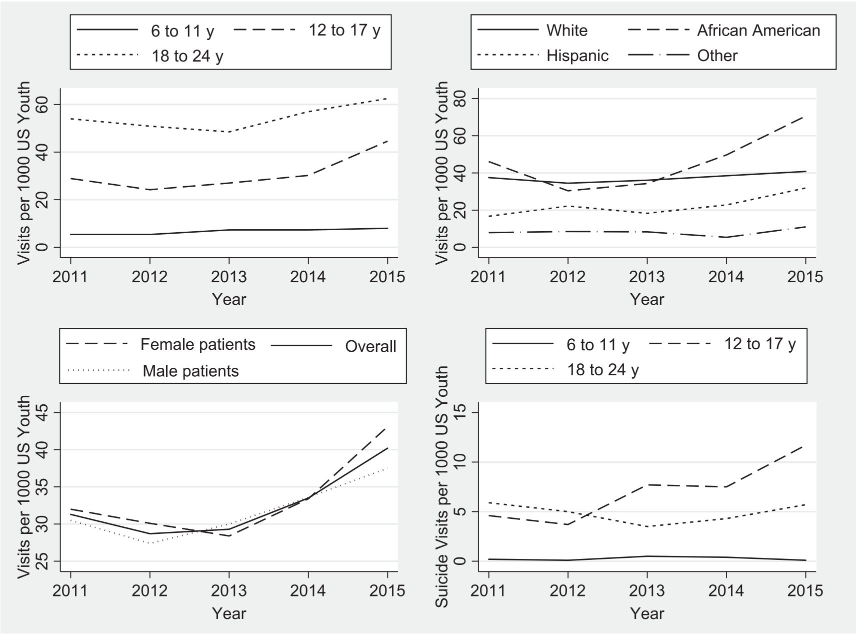

FIGURE 1

Age, race, and sex trends in psychiatric and suicide-related ED visits.

Variables

Identification of Psychiatric ED Visits

The primary study outcome was probability of a psychiatric ED visit. These visits were identified on the basis of the following: (1) diagnoses classified by using the *International Classification of Diseases, Ninth Revision* codes[29] and (2) reason for visit (RFV) (record of the patient's reason for visiting the ED).

Psychiatric ED visits were identified when any of the 3 RFV or ICD-9 codes were used to identify a psychiatric disorder, psychiatric RFV, or a mental health procedure. Psychiatric diagnoses, RFVs, and procedures were identified by using preestablished criteria by researchers from the National Center for Health Statistics (NCHS).[16] Visits were classified as mood (ie, depression, mania and/or hypomania, or anxiety), behavioral (ie, aggression or conduct problems), substance use disorder (SUD), psychosis, or other psychiatric reasons (ie, personality disorder or a mental health procedure). For suicide attempt and intentional self-harm, these visits were identified separately by using RFV (5818.0, 5820.0, and 5820.1) and V codes (V62.84).[16]

Demographic Characteristics

Demographic variables related to the child included age, US region, sex (male or female) and race and/or ethnicity (a 4-level variable created by the NCHS; see Table 1 for details).

TABLE 3 Race- and Ethnicity-Related Characteristics of Psychiatric ED Visits Among Youth in the United States

	Non-Hispanic White	Non-Hispanic African American	Hispanic	Non-Hispanic Other
Count of total visits (weighted)	75 572 719	35 939 326	27 564 070	3 874 405
Count of psychiatric ED visits (weighted)	8 162 101	2 607 369	2 074 122	297 994
Estimated youth in the United States, 2011–2015	217 594 589	56 413 412	92 679 177	36 265 765
Psychiatric ED visits, % of all visits (count)*				
2011	9.3 (1 629 561)	6.3 (519 859)	5.7 (309 237)	6.2 (57 349)
2012	9.3 (1 499 311)	4.9 (342 599)	6.5 (411 193)	7.1 (61 684)
2013	9.8 (1 576 000)	5.9 (387 165)	6.1 (339 747)	7.9 (60 165)
2014	10.1 (1 682 520)	6.0 (562 364)	7.2 (423 844)	5.5 (39 253)
2015	10.3 (1 774 709)	10.8 (795 382)	9.1 (590 101)	8.9 (79 543)
Psychiatric ED visits per 1000 US youth				
2011	37.5	46.1	16.7	7.9
2012	34.5	30.4	22.2	8.5
2013	36.1	34.3	18.3	8.3
2014	38.5	49.7	22.8	5.4
2015	40.8	70.6	31.9	11.0
Region,* % of all psychiatric ED visits				
Northeast	19.8	19.4	21.1	24.1
Midwest	28.1	26.8	11.8	19.3
South	32.7	44.0	24.7	24.8
West	19.4	9.8	43.1	31.8
Youth, %				
6–11	5.6	7.2	6.6	13.6
12–17	27.9	28.9	37.1	27.6
18–24	66.5	63.9	56.3	58.8
Sex, %				
Female	51.8	47.3	47.6	45.3
Male	48.2	52.7	52.4	54.6
Insurance,* %				
Private	41.7	18.6	22.6	40.4
Public	37.5	54.3	56.0	35.6
Self-pay	15.1	19.7	14.6	9.4
Other	5.7	7.4	6.8	14.5
Visit on a weekend,* %				
No	73.4	74.5	76.8	69.1
Yes	26.6	25.5	23.2	30.9
Arrival time,* %				
Morning (<11 AM)	29.4	26.6	25.2	27.4
Afternoon (11 AM–4 PM)	28.7	31.5	32.7	26.9
Evening (5 PM–12 AM)	41.9	41.9	42.1	45.7
Urgent*				
No	28.3	37.5	27.8	32.4
Yes	71.7	62.4	72.2	67.6
Length of visit, %				
<90 min	20.9	20.5	17.3	25.7
90–179 min	30.6	25.9	25.0	16.5
180–359 min	28.3	28.4	35.6	27.9
≥6 h	20.2	25.2	22.1	29.9
Arrive by ambulance,* %				
No	24.0	28.2	27.4	36.0
Yes	76.0	71.8	72.5	64.0
Mental health provider seen, %				
No	82.7	84.6	84.5	92.1

Visit Characteristics

A host of visit-related descriptors were available. These included insurance type, time of day, day of visit, whether a mental health professional was seen during the visit, whether the patient arrived via ambulance, and urgency of visit (dichotomized as urgent [emergent, immediate, and urgent] versus not [semiurgent and not urgent]). Length of visit was grouped in quartiles. Disposition or whether the visit resulted in a hospitalization was classified as either admission to a medical unit, admission to a psychiatric unit, or other (eg, discharge from the hospital). See Table 1 for details.

Missing Data

Prevalent missing data (>5%) were observed for urgency of visit (22%), race and/or ethnicity (21%), and insurance type (8%). Imputation procedures, conducted by the NCHS,[30] were used for race and/or ethnicity only. In the multivariate analyses, a missing data indicator was included for each of these variables (excluding race and/or ethnicity) for the purposes of retaining the full sample.

Analysis

Trends in psychiatric ED visits are reported as proportions (number of psychiatric ED visits over total ED visits) and counts by using the NHAMCS data. Rates (visits per 1000 youth in the United States) and ratios of rates (reflecting percent change) were calculated by using the census data. To address the first study question, a logistic regression model was used to examine changes in the odds of a psychiatric ED visit over time among youth 6 to 24 years of age. For the second study question, separate logistic models were used to test whether there was an increase in the odds of a psychiatric ED visit over time for each individual age, sex, and

TABLE 3 Continued

	Non-Hispanic White	Non-Hispanic African American	Hispanic	Non-Hispanic Other
Yes	17.3	15.4	15.5	8.0
Admit to hospital, %				
No	80.5	81.8	84.0	80.3
Yes or transfer to another hospital	9.8	7.6	6.5	13.0
Transfer or admit to a psychiatric facility	9.7	10.6	9.5	6.8
Psychiatric diagnoses or RFV,[*,a] %				
Mood	54.0	47.4	51.6	63.4
Behavior[*]	11.9	18.6	16.9	6.7
SUD[*]	43.7	37.1	35.6	24.1
Psychosis	6.2	9.3	5.7	2.7
Suicide attempt or self-injury	12.9	11.4	12.8	20.2
Other	29.7	33.0	27.5	36.4
Count of psychiatric diagnoses or RFVs, mean[*]	1.45	1.45	1.37	1.33
Primary diagnosis is psychiatric,[*] %				
No	32.8	35.2	37.9	37.7
Yes	67.2	64.8	62.1	62.3

[a] Reflects the presence of any of the listed diagnoses or RFVs.

[*] $P < .05$.

racial and/or ethnic group (for a total of 9 separate models).

For the third study question, a series of regression models were employed to identify differences in the demographic and visit-related factors associated with age, sex, and race and/or ethnicity. These analyses were limited to psychiatric ED visits only, with the group (age, sex, or race) serving as the outcome variable. For sex, a logistic regression model was employed, whereas a multinomial regression model was used for age and race and/or ethnicity because there were multiple discreet categories. As an example, the relative risk ratio for evening (from the multinomial model; see Table 2) can be interpreted as the relative probability of a psychiatric visit occurring in the evening (rather than the morning), is 2.35 times more likely to occur among children compared with young adults.

All models used to assess predictors of psychiatric ED visits included year, region, sex, arrival time, weekend (versus weekday), and insurance type as covariates. All other variables (eg, arrival by ambulance, urgency, length of visit, and diagnosis) were examined sequentially in individual models to avoid problems with multicollinearity. All regression models were examined at the visit level (by using the NHAMCS) among those with and/or without psychiatric needs. Whole population data from the census were not included in the models. All analyses were conducted in Stata 15.0 (Stata Corp, College Station, TX) by using the survey sampling weights.

RESULTS

Overall Trends in Psychiatric ED Visits

Table 1 displays the 5-year trends in psychiatric ED visits by age group. Overall, there was a significant increase in the odds of a visit over time (odds ratio [OR]: 1.07; 95% confidence interval [CI]: 1.01 to 1.13; $P = .01$). Shown in Fig 1 and Table 1, increasing rates of psychiatric ED visits among youth in the United States (from 31.3 to 40.2 per 1000; a 28% increase) was also supported.

Age Trends in Psychiatric ED Visits

For children, there was no significant change over time in the probability of a psychiatric ED visit (OR: 1.05; 95% CI: 0.92 to 1.21; $P = .44$). There was a rise (5.2–8.0 psychiatric ED visits per 1000 US children; a 53% increase) by using whole population data as the denominator, which do not take into account the increase in ED visits overall.

For adolescents, psychiatric ED visits were much more likely than for children (OR: 4.62; 95% CI: 3.73 to 5.72; $P < .001$). Young adults were also much more likely to visit the ED for psychiatric purposes compared with children (OR: 4.93; 95% CI: 3.99 to 6.10; $P < .001$), although there was no difference when compared with adolescents (OR: 1.07; 95% CI: 0.92 to 1.23; $P = .37$). Notably, young adults had the highest overall population rates.

The probability of a psychiatric ED visit significantly increased over time for adolescents (OR: 1.11; 95% CI: 1.02 to 1.21; $P = .01$) and young adults (OR: 1.08; 95% CI: 1.01 to 1.15; $P = .03$). By using census data, a larger increase was observed for adolescents (28.9–44.6 psychiatric ED visits per 1000 youth in the United States; a 54% increase) than for young adults (54.0–62.4 per 1000 youth in the United States; a 15% increase). See Table 1 for details.

Race and/or Ethnicity Trends in Psychiatric ED Visits

Table 3 reveals trends in psychiatric ED visits across racial and ethnic groups. No significant change in the odds of a psychiatric ED visit was observed over time for the white group (OR: 1.03; 95% CI: 0.97 to 1.10; $P = .31$). However, a significant increase was observed among those in the African American (OR: 1.16; 95% CI: 1.03 to 1.30; $P = .01$) and Hispanic groups (OR: 1.12; 95% CI: 1.01 to 1.24; $P = .02$). Both of these findings remained significant even after adjusting for insurance status.

TABLE 4 Sex-Related Characteristics of Psychiatric ED Visits Among Youth in the United States

	Female Sex	Male Sex
Count of total visits (weighted)	87 687 560	68 404 546
Count of psychiatric ED visits (weighted)	6 582 345	6 559 241
Estimated youth in the United States, 2011–2015	196 847 905	206 105 038
Psychiatric ED visits*, % of all visits (count)		
2011	6.9 (1 259 925)	8.9 (1 256 081)
2012	6.9 (1 184 067)	8.6 (1 130 720)
2013	6.7 (1 122 287)	10.0 (1 240 790)
2014	7.4 (1 320 195)	9.4 (1 387 786)
2015	9.5 (1 695 871)	11.0 (1 543 864)
Psychiatric ED visits per 1000 US youth		
2011	32.0	30.5
2012	30.1	27.4
2013	28.4	30.0
2014	33.4	33.6
2015	43.1	37.5
Region,* % of all psychiatric ED visits		
Northeast	18.8	21.3
Midwest	24.8	25.1
South	37.8	29.2
West	18.8	24.5
Youth,* y, %		
6–11	3.6	9.0
12–17	33.4	25.6
18–24	63.0	65.4
Race, %		
Non-Hispanic white	64.2	60.0
Non-Hispanic African American	18.7	20.9
Hispanic	15.0	16.6
Non-Hispanic other	2.1	2.5
Insurance, %		
Private	34.1	34.5
Public	46.4	40.6
Self-pay	14.5	17.0
Other	5.0	7.9
Visit on a weekend, %		
No	73.4	74.6
Yes	26.5	25.4
Arrival time, %		
Morning (<11 AM)	28.2	28.1
Afternoon (11 AM–4 PM)	31.6	28.1
Evening (5 PM–12 AM)	40.2	43.8
Urgent, %		
No	31.7	28.4
Yes	68.2	71.6
Length of visit, %		
<90 min	20.8	19.9
90–179 min	28.4	28.5
180–359 min	29.5	29.4
≥6 h	21.2	22.2
Arrive by ambulance, %		
No	25.4	25.9
Yes	74.6	74.1
Mental health provider seen, %		
No	82.5	84.5
Yes	17.4	15.4
Admit to hospital, %		
No	81.9	80.7
Yes or transfer to another hospital	7.4	10.4
Transfer or admit to a psychiatric facility	10.7	8.9
Psychiatric diagnosis or RFV,*,[a] %		
Mood*	59.1	45.9

No difference was found among the "other" race group (OR: 1.06, 95% CI: 0.84 to 1.35, *P* = .59). The census data supported increasing rates among African American (46.1–70.6 per 1000 youth, a 53% increase) and Hispanic patients (16.7–31.9, a 91% increase), whereas these rates remained flat among non-Hispanic white patients (37.5–40.8; a 9% increase) and rare among all in the "other" racial category (7.9–11.0; a 39% increase).

Sex Trends in Psychiatric ED Visits

Table 4 reveals trends in psychiatric ED visits stratified by sex. There was a slight increase in the probability over time for female patients (OR: 1.08; 95% CI: 1.01 to 1.16; *P* = .02). No significant time trends were observed for male patients (OR: 1.06; 95% CI: 0.99 to 1.13; *P* = .08). The probability of a psychiatric ED visit was increased in male patients compared with female patients (OR: 1.30; 95% CI: 1.17 to 1.45). Rates per 1000 youth also increased slightly more for female patients (32.0–43.1; a 34% increase) than for male patients (30.5–37.5; a 23% increase).

Correlates of Psychiatric ED Visits

Age Group

Child and visit-related characteristics of psychiatric ED visits across age groups are shown in Table 1. In the multivariate analyses (Table 2), children and adolescents were both less likely to have self-pay insurance, arrive by ambulance, and have an SUD diagnosis compared with young adults. Children visiting the ED were also less likely to live in the West and have a visit on the weekend compared with young adults. Both children and adolescents were more likely to have an evening visit; and adolescents only were more likely to have an afternoon visit and less likely to have the "other" insurance type (all $P < .05$).

Adolescents who visited the ED were more likely to be Hispanic, have an

TABLE 4 Continued

	Female Sex	Male Sex
Behavior	12.1	15.3
SUD*	37.1	44.2
Psychosis*	5.1	8.2
Suicide attempt or self-injury	14.6	10.9
Other	30.1	30.3
Count of psychiatric diagnoses or RFVs, mean	1.44	1.44
Primary diagnosis is psychiatric, %		
No	35.1	33.4
Yes	64.9	66.6

[a] Reflects the presence of any of the listed diagnoses or RFVs

* $P < .05$

urgent visit, see a mental health provider, and be transferred or admitted to a psychiatric facility compared with young adults. In terms of diagnoses, adolescents were more likely to have a primary psychiatric diagnosis related to the visit along with an increasing number of diagnoses. Adolescents were also more likely to have a mood, behavioral, suicide, and other diagnosis or RFV compared with young adults (all: $P < .05$). Children were far more likely to have a behavioral diagnosis or RFV and slightly more likely to have an "other" diagnosis. See Table 2 for details.

Race and/or Ethnicity

Characteristics of psychiatric ED visits across racial and/or ethnic groups are shown in Table 3. In the multivariate analyses (Table 5), white patients served as the reference group. African American patients were less likely to have a visit in the Western region of the United States, have a visit that was deemed urgent, and present with an SUD. They were more likely to have an insurance type other than private and have a behavioral problem coded as a diagnosis or RFV. Hispanic patients were less likely to have a visit occur in the Midwest and had a fewer number of diagnoses coded for their visit, whereas they were more likely to have a visit in the Western part of the United States and have public or self-pay insurance. The only significant difference for the "other" racial group was that they were less likely to have an SUD associated with their visit (all: $P < .05$).

Sex

Differences between male and female patients, in terms of demographic and visit-related characteristics of psychiatric ED visits, are shown in Table 4. In the multivariate models (Table 6), male patients were more likely to be younger and visit the ED for an SUD or psychosis compared with female patients. On the other hand, psychiatric ED visits were less likely to occur in the South among male patients.

Suicidal-Attempt or Self-Injurious Visit

Changes in the proportion of suicide-related visits (overall and within psychiatric visits) over time are shown in Table 7; population-based rates are also provided. Overall, there was an increase in the probability of a suicidal, self-injurious visit among adolescents only (OR: 1.27; 95% CI: 1.10 to 1.48; $P < .01$); there was no increase over time for children or young adults (both: $P > .80$). There was also no significant increase in the probability of a suicide-related visit for female (OR: 1.11; 95% CI: 0.97 to 1.27) or male patients (OR: 1.15; 95% CI: 0.96 to 1.37) when examined separately. When whole population rates were employed, similar increases were observed among female (4.4–6.7 per 1000 US youth; a 52% increase) and male patients (3.2–5.1; a 59% increase). Racial and/or ethnic trends were not examined because of small sample sizes.

DISCUSSION

In the current study, we found that psychiatric visits to the ED among youth 6 to 24 years of age are increasing across the United States. The largest rise in such visits were found among adolescents and youth of color. It should be noted that the findings were heavily driven by 2015, in which the largest increase in visits was observed. Nevertheless, these data reflect a continuation of historical trends in pediatric psychiatric ED visits[12,16] and are in line with recent increases in inpatient psychiatric hospitalizations.[31] Ultimately, it is unclear if the findings represent a change in identification (by providers) or reporting (by patients or family members) of mental health in the ED, a shift in the epidemiology of psychiatric disorders in the United States, or fluctuations in referral patterns or service-seeking behavior.

This study unmistakably reveals that adolescents are a population with urgent mental health needs. Not only were their visits the most acute, but their probability of suicidal attempt and/or self-harm increased as well. The latter is consistent with the national trends in suicide ideation.[22] Surprisingly, only 37% of visits involving adolescents who visited the ED for a suicidal attempt and/or self-injury resulted in a mental health provider being seen. In the same vein, only 16% of all psychiatric ED visits resulted in a mental health provider being seen. This is not the first study to identify this gap (for suicide-related or general psychiatric ED visits), which is likely due to the limited access of mental health providers in the ED.[4,5] With the growing presence of mental health in this setting, coupled with the length of these visits, this finding represents a missed opportunity for

TABLE 5 Multivariate Analysis of Correlates of Psychiatric ED Visits Among Racial and Ethnic Groups

	African American		Hispanic		Other	
	RRR	95% CI	RRR	95% CI	RRR	95% CI
Year	1.14*	1.03 to 1.27	1.10	0.98 to 1.24	1.00	0.77 to 1.30
Age group, y						
6–11	Reference	Reference	Reference	Reference	Reference	Reference
12–17	0.86	0.50 to 1.46	1.37	0.68 to 2.76	0.43	0.08 to 2.40
18–24	0.77	0.49 to 1.21	0.78	0.38 to 1.58	0.35	0.07 to 1.73
Region						
Northeast	Reference	Reference	Reference	Reference	Reference	Reference
Midwest	0.93	0.52 to 1.69	0.35*	0.20 to 0.61	0.59	0.15 to 2.39
South	1.45	0.85 to 2.50	0.73	0.41 to 1.27	0.65	0.23 to 1.77
West	0.49*	0.26 to 0.95	2.11*	1.31 to 3.41	1.35	0.66 to 2.81
Sex						
Female	Reference	Reference	Reference	Reference	Reference	Reference
Male	1.26	0.99 to 1.61	1.15	0.83 to 1.59	1.08	0.58 to 2.01
Insurance						
Private	Reference	Reference	Reference	Reference	Reference	Reference
Public	3.36*	2.23 to 5.05	2.72*	1.85 to 4.00	0.97	0.35 to 2.72
Self-pay	2.99*	1.81 to 4.92	2.42*	1.48 to 3.93	0.77	0.28 to 2.07
Other	2.93*	1.56 to 5.50	1.84	0.91 to 5.02	2.68	0.98 to 4.53
Visit on a weekend						
No	Reference	Reference	Reference	Reference	Reference	Reference
Yes	1.01	0.72 to 1.42	0.87	0.59 to 1.26	1.31	0.65 to 2.63
Arrival time						
Morning (<11 AM)	Reference	Reference	Reference	Reference	Reference	Reference
Afternoon (11 AM–4 PM)	1.00	0.69 to 1.44	1.13	0.73 to 1.77	0.97	0.41 to 2.31
Evening (5 PM–12 AM)	1.01	0.73 to 1.42	1.06	0.72 to 1.56	1.10	0.53 to 2.31
Urgent						
No	Reference	Reference	Reference	Reference	Reference	Reference
Yes	0.67*	0.45 to 0.97	0.89	0.39 to 2.01	0.94	0.41 to 2.14
Length of visit	1.13	0.99 to 1.28	1.08	0.96 to 1.21	0.98	0.71 to 1.36
Arrive by ambulance						
No	Reference	Reference	Reference	Reference	Reference	Reference
Yes	1.30	0.94 to 1.80	1.23	0.85 to 1.75	1.88	0.85 to 4.16
Mental health provider seen						
No	Reference	Reference	Reference	Reference	Reference	Reference
Yes	0.87	0.61 to 1.23	0.81	0.55 to 1.19	0.38	0.13 to 1.13
Admit to hospital						
No	Reference	Reference	Reference	Reference	Reference	Reference
Yes or transfer	0.80	0.52 to 1.24	0.69	0.40 to 1.20	1.35	0.50 to 3.64
Psychiatric facility	0.97	0.58 to 1.63	0.69	0.42 to 1.11	0.66	0.22 to 1.96
Psychiatric diagnosis or RFV[a]						
Mood	0.77	0.58 to 1.02	0.91	0.67 to 1.22	1.62	0.73 to 3.64
Behavior	1.60*	1.09 to 2.34	1.34	0.87 to 2.06	0.41	0.14 to 1.23
SUDs	0.74*	0.56 to 0.97	0.73	0.52 to 1.01	0.39*	0.20 to 0.69
Psychosis	1.38	0.89 to 2.50	0.78	0.44 to 1.41	0.42	0.15 to 1.13
Suicide attempt or self-injury	0.91	0.56 to 1.42	0.82	0.55 to 1.23	1.82	0.88 to 3.74
Other	1.17	0.87 to 1.57	0.80	0.55 to 1.16	1.33	0.68 to 2.62
Count of diagnoses and/or RFVs	0.94	0.78 to 1.15	0.75*	0.60 to 0.94	0.80	0.37 to 1.71
Primary diagnosis is psychiatric	0.93	0.69 to 1.27	0.76	0.52 to 1.11	1.44	−0.01 to 2.5

RRR, relative risk ratio.

[a] Reflects the presence of any of the listed diagnoses or RFVs; non-Hispanic white patients served as the reference group.

* $P < .05$.

screening and treatment planning. Nevertheless, there are promising efforts to increase the availability of expertise within the ED, notably through the use of telemedicine or other mobile health technologies and linkages to treatment afterward.[32–34] Data from this study support the continued funding and effort of these initiatives.

The rise in psychiatric ED visits among youth of color is an important finding from this study. Again, this finding was heavily driven by 2015. Although there were no visit-related differences (eg, time of day, arrival type, and urgency), there were several known demographic (eg, insurance type and geographic location) and diagnostic (eg, SUDs)

TABLE 6 Multivariate Analysis of Correlates of Psychiatric ED Visits Across Youth Sex

	Female Sex	Male Sex	
		OR	95% CI
Year	Reference	0.97	0.91 to 1.05
Age group, y			
6–11	Reference	Reference	Reference
12–17	Reference	0.29*	0.18 to 0.49
18–24	Reference	0.38*	0.54 to 0.60
Region			
Northeast	Reference	Reference	Reference
Midwest	Reference	0.95	0.74 to 1.21
South	Reference	0.67*	0.51 to 0.87
West	Reference	1.20	0.92 to 1.80
Race and/or ethnicity			
White, non-Hispanic	Reference	Reference	Reference
African American, non-Hispanic	Reference	1.26	0.99 to 1.61
Hispanic	Reference	1.14	0.83 to 1.58
Other	Reference	1.09	0.58 to 2.05
Insurance			
Private	Reference	Reference	Reference
Public	Reference	0.81	0.62 to 1.06
Self-pay	Reference	1.17	0.78 to 1.78
Other	Reference	1.53	0.99 to 2.40
Visit on a weekend			
No	Reference	Reference	Reference
Yes	Reference	0.94	0.77 to 1.67
Arrival time			
Morning (<11 AM)	Reference	Reference	Reference
Afternoon (11 AM–4 PM)	Reference	0.89	0.67 to 1.19
Evening (5 PM–12 AM)	Reference	1.09	0.84 to 1.42
Urgent			
No	Reference	Reference	Reference
Yes	Reference	1.25	0.97 to 1.61
Length of visit	Reference	1.00	0.99 to 1.00
Arrive by ambulance			
No	Reference	Reference	Reference
Yes	Reference	0.99	0.79 to 1.22
Mental health provider seen			
No	Reference	Reference	Reference
Yes	Reference	0.89	0.70 to 1.13
Admit to hospital			
No	Reference	Reference	Reference
Yes or transfer to another hospital	Reference	1.54	1.08 to 2.20
Transfer or admit to a psychiatric facility	Reference	0.90	0.65 to 1.25
Psychiatric diagnosis or RFV			
Mood	Reference	0.60	0.48 to 75
Behavior	Reference	1.28	0.91 to 1.78
SUDs	Reference	1.41*	1.13 to 1.75
Psychosis	Reference	1.70*	1.11 to 2.61
Suicide attempt or intentional self-injury	Reference	0.75	0.52 to 1.06
Other	Reference	1.02	0.79 to 1.33
Count of diagnoses and/or RFVs	Reference	1.03	0.89 to 1.20
Primary diagnosis is psychiatric			
No	Reference	Reference	Reference
Yes	Reference	1.14	0.91 to 1.43

* *P* < .05

differences between racial and ethnic groups.[35] Future research is needed to unpack these findings, particularly among African American youth who had less urgent visits.

A few sex-related differences were identified in this study. Although there was no difference in time trends, male patients were slightly more likely to visit the ED for psychiatric reasons, which departs from previous pediatric research.[11] This discrepancy is likely due to the inclusion of young adults, who had the highest proportion of substance use–related ED visits. In this study and others, male patients are known to have increased rates of substance abuse compared with female patients.[35] Surprisingly, female patients were not significantly more likely to visit the ED for suicide or self-injury, a finding that may be partly due to the small samples sizes given the rarity of these visits.[36] This finding supports the need for suicide prevention and interventions efforts among male patients as well as female patients, who could be overlooked.

Although many researchers and clinicians look to the outpatient mental health system to prevent psychiatric ED visits, there is mixed evidence to suggest that a connection to mental health providers can reduce such visits.[37,38] For instance, a recent systematic review revealed little to no evidence that engagement in outpatient, primary care, or community and/or school-based mental health services impacted ED use.[37] One explanation may be that providers themselves may be sending children to the ED during times of crisis, as reflected by a recent national survey that revealed that 60% of child and adolescent psychiatrists recommended that parents take their child to the ED during times of crisis.[39] Although the ultimate goal is to link youth with appropriate sources of care outside of the ED (particularly because these visits have been linked to iatrogenic outcomes,[40] poor follow-up,[41] and repeat visits[42]), the ED will likely have to play a continued role in treating both acute and chronic mental health issues in the future. As such, this study supports the continued effort to outfit EDs with the expertise to identify and treat mental health problems, to investigate novel approaches to crisis intervention (eg, mobile crisis centers, peer crisis

TABLE 7 Trends in ED Visits Related to Suicidal Attempts and/or Self-Injury

	2011	2012	2013	2014	2015	Overall
All ED visits, %						
6–11 y	<0.1	<0.1	0.2	0.1	<0.1	<0.1
12–17 y*	1.4	1.3	2.7	2.3	3.5	2.2
18–24 y	1.3	1.0	0.7	0.8	1.1	0.9
Female patients	1.0	1.0	1.1	1.0	1.5	1.1
Male patients	0.9	0.7	1.1	1.1	1.5	1.0
Overall*	0.9	0.8	1.1	1.0	1.5	1.7
Psychiatric visits only, %						
6–11 y	4.2	2.4	7.3	5.3	1.7	4.2
12–17 y*	15.8	15.5	28.7	24.8	26.2	22.7
18–24 y	10.9	9.9	7.1	7.6	9.1	8.9
Female patients	13.6	13.8	15.9	13.9	15.5	14.6
Male patients	10.4	7.9	11.0	10.6	13.5	10.9
Overall	12.0	10.9	13.3	12.2	14.5	12.7
Visits per 1000 US youth						
6–11 y	0.2	0.1	0.5	0.4	0.1	0.3
12–17 y	4.6	3.7	7.7	7.5	11.7	7.1
18–24 y	5.9	5.0	3.5	4.3	5.7	4.8
Female patients	4.4	4.1	4.5	4.6	6.7	4.9
Male patients	3.2	2.2	3.3	3.6	5.1	3.5
Overall	3.7	3.2	3.9	4.1	5.8	4.2

* $P < .05$.

services, crisis stabilization beds, and telemedicine crisis services),[43,44] or to design new models of urgent mental health care that are accessible (particularly in the evening).

There are several study limitations that require mentioning. First, there were missing data across a few variables, namely visit acuity and race and/or ethnicity, although the latter was imputed by the NCHS.[30] The inability to confirm diagnostic validity is another limitation because consistent application of diagnostic criteria may systematically vary (across providers and over time) in unknown ways. These limitations are offset by the nationally representative sample, in-depth analysis across numerous variables, and novel findings that have important implications to both policy and practice.

CONCLUSIONS

Psychiatric ED visits among young people increased nationally, most notably in 2015. The largest increases were observed among adolescents and youth of color, whereas young adults had the highest overall population rates. Visits related to suicidal attempt and self-injury also increased among adolescents. These data support the continued funding and deployment of evidenced-based interventions that can effectively reach families and young adults during times of crisis.

ABBREVIATIONS

CI: confidence interval
ED: emergency department
NCHS: National Center for Health Statistics
NHAMCS: National Hospital Ambulatory Medical Care Survey
OR: odds ratio
RFV: reason for visit
SUD: substance use disorder

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Trends in Psychiatric Emergency Department Visits Among Youth and Young Adults in the US

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WIC Food Package Changes: Trends in Childhood Obesity Prevalence

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abstract

OBJECTIVES: To evaluate the association of the 2009 changes to the US Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) food package and childhood obesity trends. We hypothesized that the food package change reduced obesity among children participating in WIC, a population that has been especially vulnerable to the childhood obesity epidemic.

METHODS: We used an interrupted time-series design with repeated cross-sectional measurements of state-specific obesity prevalence among WIC-participating 2- to 4-year-old children from 2000 to 2014. We used multilevel linear regression models to estimate the trend in obesity prevalence for states before the WIC package revision and to test whether the trend in obesity prevalence changed after the 2009 WIC package revision, adjusting for changes in demographics. In a secondary analysis, we adjusted for changes in macrosomia and high prepregnancy BMI.

RESULTS: Before the 2009 WIC food package change, the prevalence of obesity across states among 2- to 4-year-old WIC participants was increasing by 0.23 percentage points annually (95% confidence interval: 0.17 to 0.29; $P < .001$). After 2009, the trend was reversed (-0.34 percentage points per year; 95% confidence interval: -0.42 to -0.25; $P < .001$). Changes in sociodemographic and other obesity risk factors did not account for this change in the trend in obesity prevalence.

CONCLUSIONS: The 2009 WIC food package change may have helped to reverse the rapid increase in obesity prevalence among WIC participants observed before the food package change.

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WHAT'S KNOWN ON THIS SUBJECT: Changes to the Special Supplemental Nutrition Program for Women, Infants and Children (WIC) in 2009 decreased intake of foods and beverages associated with excess weight gain. Surveillance data suggest obesity prevalence among WIC-participating children declined from 2010 to 2014.

WHAT THIS STUDY ADDS: We quantify the association of the WIC package change and childhood obesity using a quasi-experimental study design and accounting for state-level differences, race and/or ethnicity, poverty trends, and trends in macrosomia and high prepregnancy BMI among WIC participants.

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The Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) provides vouchers for nutrient-dense foods and beverages to more than half of all US infants and one-quarter of low-income pregnant and postpartum women and children <5 years of age.[1,2] To be eligible, households must have an income ≤185% of the federal poverty level or participate in several other federal aid programs and be at nutritional or medical risk.[3] In addition to being at risk for poor nutritional status, WIC-eligible children have also been particularly vulnerable to the childhood obesity epidemic.[4]

In 2009, the lists of foods that could be purchased with WIC vouchers (known as the WIC food packages), which includes basic food categories, including milk, cheese, beans, peanut butter, eggs, juice, cereal, and grains, were updated to better align with dietary guidelines. The new package provides extra cash allowances for fruits and vegetables, cuts the previous juice allowance in half, requires low-fat or skim milk for 2- to 4-year-olds, reduces cheese, and requires whole-grain instead of refined-grain products (among other changes).[2] Evidence suggests the revised WIC package has beneficially impacted household diets, including an increase in Healthy Eating Index scores,[5] reductions in juice purchases, and increases in the intake of fruit and whole grains.[6] A recent analysis of Nielsen Homescan Consumer Panel data found that WIC households' purchases of total calories declined by 11% after the package change, whereas purchases of fruits and vegetables increased.[7]

On the basis of these well-documented improvements in nutrition after the WIC package change, the risk of childhood obesity among WIC-participating children may also have declined. The Centers for Disease Control and Prevention (CDC) reported a decline in the prevalence of obesity and severe obesity among WIC-participating children from 2010 to 2014 but did not directly test whether the WIC package change was associated with a change in childhood obesity trends.[8] Given the variation in childhood obesity rates by state,[9] evaluating longer-term trends in obesity prevalence and the potential differential impact of the WIC package change by state is critical. A focus on state-level trends is particularly important given the level of control that state WIC agencies have over program administration[1]; states had discretion for implementing certain aspects of the revised food packages and may have differed in the extent to which healthier foods were made available.[10] In this article, we evaluate whether national and state-level trends in obesity prevalence among WIC-participating 2- to 4-year-old children changed after the 2009 WIC package revision, adjusting for sociodemographic composition and other risk factors for childhood obesity.

METHODS

Study Design

This quasi-experimental study employed interrupted time-series analysis[11] by using repeated cross-sectional measurements of obesity prevalence among WIC-participating children at the state level to test the potential impact of the 2009 WIC package change on childhood obesity trends. In interrupted time-series analysis, regression models estimate trends in population measures of an outcome before a prespecified time when a policy change (or other intervention) occurs and then test whether the trend changes afterward.[11] In this study, we compared population trends in obesity prevalence among WIC-participating 2- to 4-year-olds before and after 2009 to estimate whether there were changes in obesity prevalence or changes in the trend in obesity prevalence that may be attributable to the package change.[12] To reduce confounding from other concurrent trends, such as the Great Recession of 2007 to 2009, which occurred during a similar time period as the package change and which resulted in an increase in the use of federal food assistance and new populations using such assistance, we controlled for changes in racial-ethnic composition and child poverty at the state level. In an exploratory analysis including a subsample of states with complete data, we also examined whether changes in WIC-participating children's birth weight and maternal BMI were confounders.

Measures and Data Sources

Our primary outcome is obesity prevalence, calculated as the percentage of 2- to 4-year-old children enrolled in the WIC in a given state or territory with sex-specific BMI for age ≥95th percentile on the 2000 CDC growth charts.[13] We obtained the state-level prevalence of obesity among WIC-participating 2- to 4-year-olds in 2008, 2010, 2012, and 2014 from data.gov files[14] derived from the WIC Participant and Program Characteristics (WIC-PC), a national census of participants in the WIC administered every 2 years by the US Department of Agriculture's Food and Nutrition Service.[15] In addition, we used prevalence estimates from Pan et al[13] for 2000, 2004, 2010, and 2014. In a comparison of data for the 2 years of overlap (2010 and 2014), we find negligible differences between the data sets (Supplemental Information). We excluded Hawaii from our main analyses given concerns about data quality.[8] Our data set includes data from 49 states in 6 years, or 294 observations; these data were collected from all 2- to 4-year-olds for whom obesity prevalence was determined, a group that ranged in number from 2 253 471 children in

2000 to 3 152 137 children in 2012 in total across all 49 geographies.

To account for changes in the racial-ethnic composition of the WIC population, we calculated the percentage of 2- to 4-year-old WIC participants classified as white, African American, Asian American and/or Pacific Islander, American Indian, or Hispanic for each state and year. The WIC-PC reports for 2008, 2010, 2012, and 2014 included state-level race-ethnic breakdowns for children between the ages of 2 and 4 years but not for 2000 and 2004. We obtained data on race and ethnicity for 2000 and 2004 from the WIC data[16,17]; when comparing these with the WIC-PC report data[14] for the 3 years of overlap (2008, 2010, and 2012), we found high correlations between measures of racial and ethnic makeup (Supplemental Information).

To account for possible shifts in child poverty, we assessed state-level child poverty rates with the Supplemental Poverty Measure (SPM) for children ages 0 to 17 years,[18] calculated by the Center on Poverty and Social Policy at Columbia University.[18] The SPM is a posttax measure of poverty used by the Census Bureau and the Bureau of Labor Statistics that accounts for in-kind transfers and other benefits as well as nondiscretionary expenses, such as medical or child care costs.[19] The SPM is considered an improvement over the official poverty measure in its use of a poverty threshold updated for contemporary expenditure patterns[20]; we use a measure anchored to nondiscretionary spending (for food, clothing, shelter, and utilities) from 2008 to 2012[20] and adjusted for geographic differences in costs of living.[18]

For the exploratory analysis of whether changes in the 2- to 4-year-olds' history of macrosomia or maternal prepregnancy weight status could have played a role in changes in childhood obesity prevalence among WIC-participating children, we extracted the proportions of WIC participants with a birth weight >4000 g and of WIC-participating mothers with a prepregnancy BMI classified as obese (>29.1, the cutoff used by WIC agencies before Revision 10 of the Nutrition Risk Criteria)[21] from the WIC-PC reports.[14,16,17,22–28] To address the lag between the measurement of maternal prepregnancy BMI and obesity in our population of 2- to 4-year-old children, we include prepregnancy BMI with a 4-year lag. We note that only 41 states reported data on birth weight and prepregnancy BMI in at least 2 time points, and 45.1% of state-year observations are missing data for at least 1 of the 2 variables. We assessed the robustness of our results to the use of state-level birth weight data from the CDC Wonder Database natality public-use data,[29] but these data cover all children in the United States (rather than just the WIC population), and we were unable to identify a comparable data source for prepregnancy BMI. Because of the high incidence of missing data, we consider these analyses secondary and exploratory.

Statistical Analyses

We fitted segmented linear regression models to state-level obesity prevalence data as a function of year (centered at 2009), an indicator for post–WIC-package change (ie, 1 if year >2009 and 0 if otherwise), and an interaction term of the indicator and the number of years since the change. The coefficient for year can be interpreted as the annual percentage-point change in obesity per year on average across states, whereas the coefficient for the indicator of years after 2009 represents the average percentage-point drop in obesity for all years after 2009 (a level change), and the coefficient of the interaction of the indicator and the year represents the average annual percentage-point change for each year after 2009 (a change in slope).[11] All models were fitted with state fixed effects to control for time-invariant differences in obesity prevalence between states as well as with state random effects. Hausman tests[30] fail to reject the null hypothesis of no difference in coefficient estimates from fixed- versus random-effect specifications; thus, we report results from the more efficient random-effect models. The full model specification can be found in the Supplemental Information.

We first fit baseline models including just the year, level, and trend variables as well as the random effects. The level variable was not significant, suggesting there was no immediate drop in obesity prevalence after the year 2009; this variable was thus excluded from the models. We then fit models with controls for child poverty as well as racial-ethnic composition to assess whether changes in the demographics of WIC participants could explain changes in obesity level. Lastly, for our exploratory analysis of the potential impact of changes in trends in macrosomia and prepregnancy BMI on trends in childhood obesity prevalence in this population, we fit a model including the prevalence of macrosomia and high maternal prepregnancy BMI among those states with complete data for these variables. Because complete case analysis may produce biased results when data are not missing completely at random, we further used multiple imputation by chained equations to impute missing data.[31] We imputed 20 data sets in which macrosomia and the percentage of mothers with high prepregnancy BMI were iteratively predicted with regression equations including all covariates used in our main analyses; the resultant model for this exploratory analysis was fit on each data set with results pooled to reflect the uncertainty in the predicted values.[32]

The main analyses were conducted in R 3.4.4. Fixed- and random-effects models were fitted with the plm package.[33] Sensitivity analyses and multiple imputation were conducted by using Stata 14 (Stata Corp, College Station, TX). Two-sided *P* values <.05 were considered statistically significant.

RESULTS

Demographic characteristics of WIC participants from 2000 to 2014 are presented in Table 1. The average obesity prevalence among WIC-participating 2- to 4-year-old children across the states was 12.92% in 2000, rose to an average of 15.13% in 2008, stayed roughly the same in 2010, and then decreased to 14.24% by 2014. Although the sociodemographic composition of the 2- to 4-year-old WIC-participant population changed somewhat over this period, we did not identify statistically significant differences in the state-level mean racial makeup or percentage of children in poverty. The average percentage of 2- to 4-year-old WIC participants born with macrosomia declined from 2000 to 2008 and then leveled off from 2008 to 2014. Meanwhile, the percentage of WIC-participating women who had a prepregnancy BMI >29.1 increased steadily from 2000 to 2014.

Results from the crude interrupted time-series analysis show that before 2009, national obesity prevalence among 2- to 4-year-old WIC participants was increasing 0.26 percentage points annually (95% confidence interval [CI]: 0.22 to 0.31; *P* < .001; Table 2). After 2009, the trend was reduced by 0.55 percentage points (95% CI: −0.66 to −0.43; *P* < .001). Observations are correlated within states, with ~78% of the variance being attributable to variation between states. Predictions for each of the 49 states with complete data are presented in Fig 1.

TABLE 1 State-Level Demographic and Anthropometric Characteristics of Participants in the WIC, 2000–2014

	2000	2004	2008	2010	2012	2014	*P*
Prevalence of obesity among 2-to 4-y-old WIC participants, mean (SD)	12.92 (2.40)	14.80 (2.38)	15.13 (2.19)	15.24 (2.24)	14.51 (2.27)	14.24 (2.27)	<.001
Race and/or ethnicity, %,[a] mean (SD)							
American Indian	3.14 (7.58)	3.27 (7.85)	3.62 (8.27)	3.50 (7.93)	3.63 (7.92)	3.56 (7.64)	.999
Asian American or Pacific Islander	2.10 (2.18)	2.25 (2.13)	2.35 (2.15)	2.61 (2.25)	2.94 (2.33)	3.37 (2.52)	.056
African American	21.29 (18.82)	19.82 (7.03)	19.37 (15.42)	19.19 (14.70)	19.95 (4.85)	20.75 (14.97)	.986
Hispanic	20.67 (20.34)	25.22 (21.39)	29.94 (22.15)	30.91 (21.33)	30.79 (20.81)	30.65 (20.37)	.086
White	52.79 (21.98)	49.44 (21.87)	44.72 (20.90)	43.79 (20.21)	42.70 (19.62)	41.67 (19.25)	.059
WIC-participating children with high birth wt, %,[b] mean (SD)	13.22 (2.38)	7.17 (1.78)	6.49 (1.44)	6.62 (1.59)	6.43 (1.76)	6.41 (1.68)	<.001
WIC-participating women with high prepregnancy BMI, %,[c] mean (SD)	21.95 (3.50)	26.22 (2.91)	28.55 (3.33)	29.96 (3.12)	30.66 (4.39)	32.22 (4.31)	<.001
Children in poverty, %,[d] mean (SD)	15.83 (4.36)	14.92 (3.98)	14.14 (3.91)	14.39 (4.01)	14.81 (3.99)	14.97 (4.12)	.412
Total No. 2-to 4-y-old WIC participants	2 253 471	2 550 533	2 790 527	3 206 995	3 152 137	2 915 253	—

Included were 49 states, excluding Hawaii. *P* values are from analysis of variance tests of differences in means. —, not applicable.

[a] Demographic makeup is presented as the number of children with race reported in each category as a percentage of (for 2000 and 2004) all 1- to 4-y-old children enrolled in the WIC or (for 2008–2014) all 2- to 4-y-old WIC participants as a percentage of all children for whom a race in the 5 categories was reported.

[b] The percentage of WIC-participating 1- to 4-y-old children with birth weights between 4001 and 6000 g. This measure is reported by state and local WIC agencies and thus is missing data for some states and territories (eg, *n* = 29 in 2000 and *n* = 37 in 2014).

[c] The percentage of WIC-participating pregnant women with prepregnancy BMI ≥29.1 reported with a 4-y lag. This measure is reported by state and local WIC agencies and thus is missing data for some states (eg, *n* = 33 in 4 years before 2000 and *n* = 40 4 years before 2014).

[d] Rate for children ages 0 to 17 y calculated with the anchored SPM available from the Center on Poverty and Social Policy at Columbia University for all US states.[19]

TABLE 2 Multivariate Random-Effects Models Predicting the State-Level Obesity Prevalence (Percentage Points) Among 2- to 4-Year-Old WIC Participants, 2000–2014

	Model 1	Model 2
Intercept (95% CI)	15.55*** (14.93 to 16.17)	16.01*** (15.30 to 16.71)
Annual trend[a], yrs (95% CI)	0.26*** (0.22 to 0.31)	0.23*** (0.17 to 0.29)
Change in annual trend after 2009 (95% CI)	−0.55*** (−0.66 to −0.43)	−0.57*** (−0.69 to −0.44)
Race and/or ethnicity, %[b] (95% CI)		
American Indian	—	0.07 (−0.003 to 0.14)
Asian American	—	0.19* (0.01 to 0.37)
African American	—	0.03 (−0.00 to 0.06)
Hispanic	—	0.03 (−0.001 to 0.05)
Children in poverty (standardized)[c], % (95% CI)	—	0.07 (−0.25 to 0.39)
ICC	0.78	0.75
N	294	294
N groups	49	49

Results are reported for models with state random effects; Durbin-Wu-Hausman tests fail to reject the null hypothesis of no significant differences in consistency between models with fixed and random effects. —, not applicable.

[a] The annual trend is calculated with the year centered in 2009.

[b] Demographic makeup is presented as the number of children with race reported in each category as a percentage of (for 2000 and 2004) all 1- to 4-y-old children enrolled in the WIC or (for 2008–2014) all 2- to 4-y-old WIC participants as a percentage of all children for whom a race in the 5 categories was reported. We further subtract the population-weighted mean demographic makeup from each of these variables so the intercept in model 2 can be interpreted as the mean overall obesity prevalence in 2009 for a state with a demographic makeup comparable to the demographic makeup of our population across all observations (1.14% American Indian, 3.24% Asian American and/or Pacific Islander, 19.95% African American, 44.16% Hispanic, and 31.5% white) and a child poverty rate equal to the average across state-year observations (14.84).

[c] Standardized rate for children ages 0 to 17 y calculated with the anchored SPM available from the Center on Poverty and Social Policy at Columbia University for all US states.[19]

* $P < .05$; *** $P < .001$

After adjusting for changes in racial-ethnic composition and child poverty, the results were essentially unchanged. We estimated a pre-2009 annual trend of a 0.23 percentage-point increase in childhood obesity prevalence (95% CI: 0.17 to 0.29; $P < .001$) and a post-2009 change in slope of −0.57 percentage points annually (95% CI: −0.69 to −0.44; $P < .001$). On the basis of these adjusted results, we estimated that after the package revisions in 2009, there was a decline in childhood obesity of 0.34 percentage points per year. The intraclass-correlation coefficient (ICC) was marginally reduced after controlling for sociodemographic variables (0.75), suggesting that between-state differences in sociodemographic makeup explained little of the between-state differences in obesity prevalence.

Our exploratory analysis of the potential influence of changes in macrosomia and high maternal prepregnancy BMI on trends in childhood obesity prevalence suggests that, although controlling for macrosomia and prepregnancy BMI may have slightly attenuated the change in trend, these 2 factors have little contribution to the observed drop in childhood obesity prevalence after 2009 (Supplemental Tables 3 and 4).

DISCUSSION

We found, using an interrupted time-series analysis, that the 2009 WIC package change was associated with a shift in the trend of childhood obesity prevalence among 2- to 4-year-old WIC participants from a 0.23 -percentage-point annual increase to a 0.34 percentage-point annual decrease. Changes in the racial-ethnic and income composition of the WIC population did not explain this change in trend, nor did changes in maternal prepregnancy BMI or macrosomia prevalence.

A change in the trend in obesity prevalence related to dietary changes resulting from the 2009 package change is plausible. A substantial body of evidence has shown that the dietary habits of WIC participants improved from before to after the package change. Participating families purchased 11% fewer total calories after the package change compared with before[7] and also improved overall diet quality in ways that may protect against obesity and facilitate healthier growth. Participants purchased and consumed less fruit juice, refined grains, grain-based desserts, and sugar-sweetened beverages while increasing purchases and consumption of fruits, vegetables, and whole grains.[5–7,34] This dietary pattern has been associated with less weight gain in both children and adults.[35,36] Small, beneficial reductions in total energy intake could result in small population-wide reductions in average BMI.[12,37,38]

Although overall our analysis revealed declining obesity prevalence after the package change, our results also suggest variation between states that was not explained by differences in racial-ethnic makeup or child poverty. Although the difference may be due to unmeasured heterogeneity in WIC populations across states, another possibility is that differences exist in how effectively the WIC package changes were implemented in each state. For example, recent research documents disparities across states in minimum stocking requirements for WIC-participating vendors.[10] Future researchers should evaluate whether differences in fidelity to the WIC package changes or other implementation factors may have played a role in potential differences in childhood obesity prevalence trends across the states.

Our analysis is subject to a number of limitations. We lack individual-

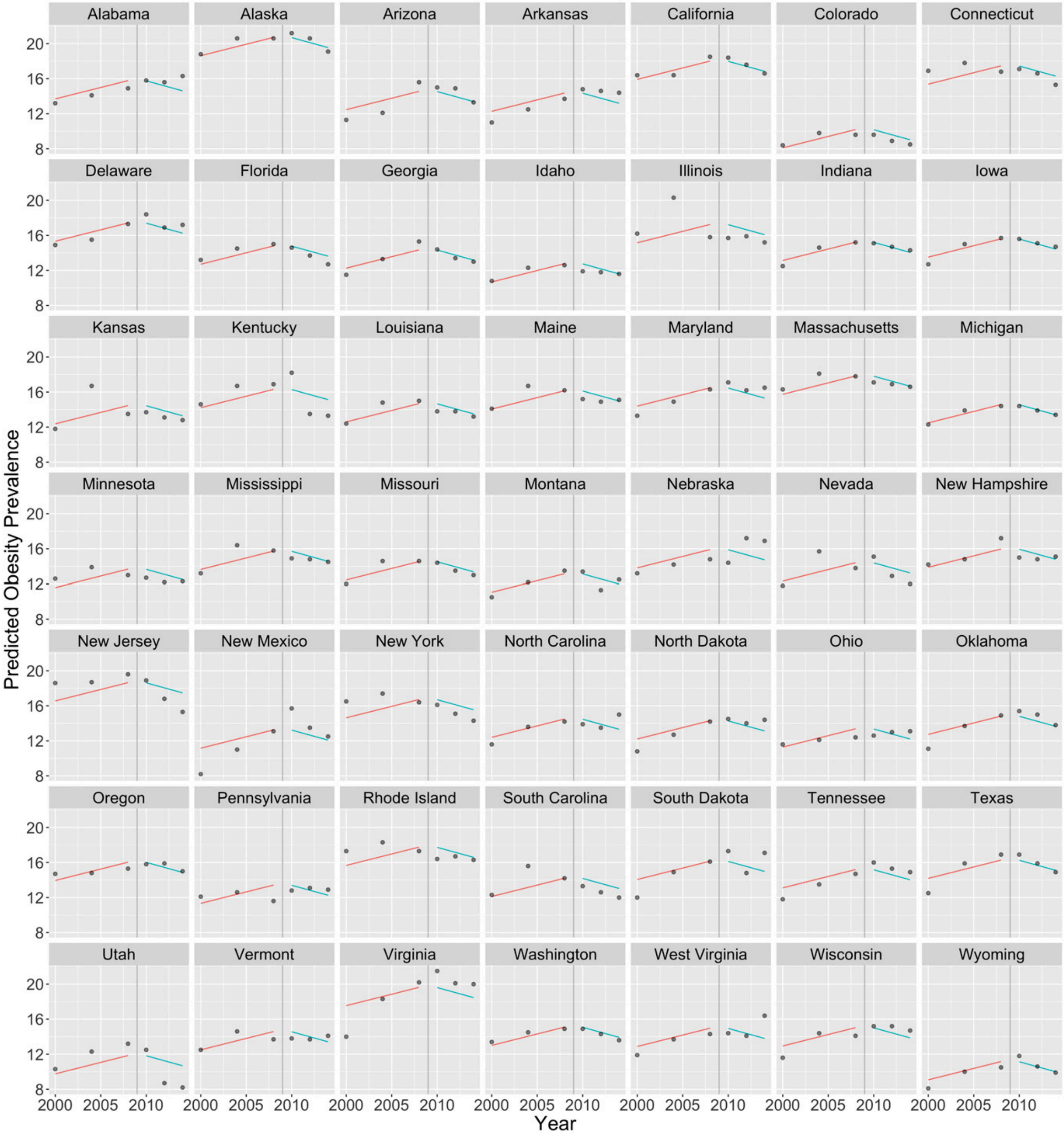

FIGURE 1

Obesity prevalence and prediction by state. Black points indicate the measured obesity prevalence among children ages 2 to 4 years in each year; lines show the fit from model 1 in Table 2, with red indicating the predicted trend before 2009 and blue indicating the trend after 2009.

level BMI data over time as well as data on how energy intake and expenditure may have changed, which would provide a mechanistic explanation of our findings. Perhaps most importantly, we are unable to control for the possibility that some other event between 2008 and 2010 may be driving the results. The Great Recession, for example, may have led to changes in the WIC population such that families who had previously had higher incomes and lower obesity risk were newly enrolling. However, we included controls for socioeconomic and demographic variables to account for these changes. Furthermore, we might expect to see changes driven by the Great Recession manifest most strongly in states that were more strongly affected, but Fig 1 does not reveal evidence of heterogeneity in the change in trend between the most strongly affected states (FL, NV, AZ, and CA) and states considered more "recession proof," such as North Dakota, South Dakota, Kansas, or Oklahoma.[39] The Patient Protection and Affordable Care Act was another major policy change in 2009, but existing evidence suggests no relationship between increased access to health insurance and obesity risk.[40,41] Although it has been suggested that the decline could be the result of other public health interventions, such as increased breastfeeding promotion in addition to that provided by WIC or obesity-prevention efforts in child care settings,[13] this is unlikely. First, carefully controlled studies suggest no causal link between breastfeeding and childhood obesity.[42–44] Second, although there are promising child care initiatives to prevent obesity,[45] these were not widely disseminated in 2009 and thus could not logically have influenced obesity trends at that point. Similarly, although the Head Start program, which also reaches 2- to 4-year-olds in poverty, has been linked with potential reductions in obesity risk,[46] there was no substantial change in Head Start in 2009 that could explain such changes in obesity trends. The inclusion of a control group of non–WIC participants would improve our ability to control for non–WIC-related policies, societal trends, or interventions that could have been impacting obesity in this population at the same time, but we are unable to identify a control group similar in age and socioeconomic characteristics to our sample because such a high proportion of low-income children participate in the WIC. Although the NHANES can provide estimates for this age group overall, the sample sizes for this age group are small once children participating in the WIC are excluded.[47] Comparing existing NHANES data on trends in childhood obesity prevalence with the WIC trends does not suggest that the overall trends in childhood obesity prevalence exactly mirrored the WIC trends. Although obesity prevalence leveled off between 2011 and 2014 for children ages 6 to 11 years, most of whom would have been too old to be affected by the WIC package change,[48] changes in the prevalence of obesity for 2- to 5-year-olds were found to have declined from 2003 to 2004 and have had no clear trend since. As more years of data as well as data on state-level differences in program implementation become available, further research should continue to evaluate the effect by, for example, examining heterogeneity in the change in trend on the basis of differences in WIC package changes by state.

CONCLUSIONS

This analysis demonstrates that the 2009 WIC package was associated with a reversal of the increasing trend in obesity prevalence among WIC participants observed from 2000 to 2014.

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ABBREVIATIONS

BMI: Body Mass Index
CDC: Centers for Disease Control and Prevention
CI: confidence interval
ICC: intraclass-correlation coefficient
SPM: Supplemental Poverty Measure
WIC: Special Supplemental Program for Women, Infants, and Children
WIC-PC: Special Supplemental Nutrition Program for Women, Infants, and Children Participant and Program Characteristics

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HPV Vaccine Delivery Practices by Primary Care Physicians

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abstract

BACKGROUND AND OBJECTIVES: To examine, among pediatricians and family physicians (FPs) (1) human papillomavirus (HPV) vaccine delivery practices, (2) delivery experiences, and (3) attitudes regarding new 2-dose HPV vaccination schedules.

METHODS: We surveyed nationally representative networks of pediatricians and FPs by Internet or mail from July 2018 to September 2018. Multivariable regression was used to assess factors associated with refusal or deferral rates of ≥50% among 11- to 12-year-old patients.

RESULTS: The response rate was 65% (302 pediatricians and 228 FPs included). Pediatricians who strongly recommended the HPV vaccine ranged from 99% for patients ≥15 years old (female) to 83% for those 11 to 12 years old (male); FPs ranged from 90% for patients ≥15 years old (female) to 66% for those 11 to 12 years old (male) ($P < .0001$ between specialties). Sixty-five percent of pediatricians and 42% of FPs always or almost always used presumptive style when discussing the HPV vaccine ($P < .0001$). Overall, 40% used standing orders and 42% had electronic alerts. Among pediatricians, the proportion reporting a refusal or deferral rate ≥50% was 19% for female patients and 23% for male patients 11 to 12 years old; FPs reported 27% and 36%, respectively. In the multivariable regression (both sexes), refusal or deferral was associated with physicians not strongly recommending the HPV vaccine to 11- to 12-year-old patients, not using a presumptive style, perceiving less resistance when introducing the HPV vaccine to a 13-year-old patient versus an 11- or 12-year-old patient, and anticipating an uncomfortable conversation when recommending the HPV vaccine to an 11- or 12-year-old patient. Eighty-nine percent of pediatricians and 79% of FPs reported that more adolescents <15 years old are completing the HPV series now that only 2 doses are recommended.

CONCLUSIONS: Although most physicians strongly recommend the HPV vaccine to 11- to 12-year-old patients, our data reveal areas for improvement in recommendation and delivery methods. Most physicians perceive that the 2-dose schedule is resulting in higher HPV completion rates.

WHAT'S KNOWN ON THIS SUBJECT: Although diseases caused by human papillomavirus (HPV) are responsible for major morbidity and mortality in the United States, HPV vaccination rates remain low. Primary care physicians' current HPV vaccine delivery practices and their experiences with HPV vaccine delivery are not well described.

WHAT THIS STUDY ADDS: Although most physicians recommend the HPV vaccine for patients 11 to 12 years old, many are not using a presumptive style when introducing the HPV vaccine, standing orders, or electronic alerts for HPV delivery. Most perceive that the 2-dose schedule is resulting in higher HPV completion rates.

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Dr Kempe conceptualized and designed the study, contributed to the data collection instrument design, and drafted the initial and final manuscripts; Drs O'Leary, Hurley, Markowitz, and Meites and Ms Lindley and Ms Stokley assisted in study design and creation of the data collection instrument and reviewed and revised the manuscript; Dr Crane conceptualized and designed the study, designed the data collection instrument, and reviewed and revised the manuscript; Ms Beaty contributed to the study design, conducted the initial and additional analyses, (Continued)

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Disease caused by human papillomavirus (HPV) remains a major public health problem globally.[1–5] Nearly all cervical and anal cancers; 63% to 75% of vulvar, vaginal, and penile cancers; and ~70%[6] of oropharyngeal cancers are attributable to HPV.[2,7–10] Annually in the United States, 33 700 new cancers are related to HPV, and 4175 women die of cervical cancer.[11]

Effective HPV vaccines have been routinely recommended at ages 11 to 12 years by the Advisory Committee on Immunization Practices (ACIP) since 2006 for girls and since 2011 for boys.[12,13] The recommendations targeting those 11 to 12 years old were based in part on facilitating implementation because other vaccines are recommended at this age. In addition, HPV vaccines are most effective when given before any HPV exposure, and vaccination at this age reaches most persons before initiation of sexual activity.

HPV vaccines have demonstrated high efficacy in preventing cervical precancers, other genital cancers, oropharyngeal cancers, and genital warts.[14] Healthy People 2020 goals include coverage of 80% for all vaccines routinely recommended for US adolescents.[15] Although these goals have been met for other adolescent vaccines, in the 2017 National Immunization Survey-Teen, HPV initiation among adolescents 13 to 17 years old was 69% for girls and 63% for boys, and series completion was only 53% for girls and 44% for boys.[16] Low HPV vaccination is related to a variety of barriers originating from health care providers and parents or patients.[17–26] Because of the crucial role of provider recommendation in parental decisions to vaccinate,[27–29] a great deal of research[21,30–36] and intervention efforts[37–40] have been focused on improving provider communication regarding HPV vaccination.

Until 2016, completion of the HPV series was defined as 3 doses over 6 months. In late 2016, the ACIP recommended a 2-dose schedule for adolescents who initiate the HPV vaccination series at ages 9 through 14 years.[23] In the 2-dose schedule, the first and second doses of the HPV vaccine should be administered at least 6 to 12 months apart.[23] Three doses remain recommended for persons who initiate the series at ages 15 through 26 years and for persons who are immunocompromised. In the context of continued suboptimal vaccination rates and recent changes to recommendations, our objectives were to examine the following among nationally representative panels of pediatricians and family physicians (FPs): (1) current delivery and communication practices regarding the HPV vaccine; (2) attitudes toward and experiences with HPV vaccine delivery; (3) rates of refusal or deferral of the HPV vaccine; (4) perceived barriers to delivery of the HPV vaccine; and (5) knowledge, practices, and attitudes regarding the 2-dose HPV vaccination schedule.

METHODS

From July 2018 to September 2018, we administered surveys to national networks of physicians who had agreed to participate in surveys about vaccine policy issues. The Colorado Multi-institutional Review Board approved this study as exempt research.

Study Setting and Population

As part of the Vaccine Policy Collaborative Initiative, a rapid survey mechanism used to assess physician attitudes about vaccine issues, we surveyed members of networks of pediatricians and FPs recruited from the memberships of the American Academy of Pediatrics (AAP) and the American Academy of Family Physicians (AAFP). Physicians were eligible if they spent ≥50% of their time providing primary care. We performed quota sampling[24] to ensure networks were similar to the AAP and AAFP memberships with respect to region, urban versus rural location, and practice setting. In previous work, we demonstrated that survey responses from network physicians were similar to those of physicians randomly sampled from American Medical Association physician databases with respect to reported demographic characteristics, practice attributes, and attitudes about vaccination issues.[24]

Survey Design

We used 4-point Likert scales to assess physicians' strength of recommendation of the HPV vaccine for patients in different age groups, physicians' frequency of using different vaccine discussion styles, physicians' perceived barriers to vaccination and extent of agreement with statements about the change from a 3-dose to a 2-dose schedule in younger teenagers, and physicians' experiences with HPV vaccine delivery. Physicians were classified as using a "presumptive"[41] (or "announcement")[30] style if they reported almost always or always introducing the HPV vaccine by saying, "We've got 3 vaccines today: Tdap, HPV and meningococcal vaccines." Physicians were classified as using a "conversational"[30,41] (or "participatory")[41] style if they reported almost always or always saying, "Are you interested in getting HPV vaccine for your child today?" National advisory panels of 6 AAP members and 6 AAFP members representing different states pretested the survey, and it was then pilot tested among 13 pediatricians and 10 FPs.

Survey Administration

The survey was administered July 2018 to September 2018, through the Internet or US mail, depending on physician preference. We sent the Internet group an initial e-mail with

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up to 8 e-mail reminders, and we sent the mail group an initial mailing and up to 2 additional mail reminders. Nonrespondents in the Internet group were also sent up to 2 mail surveys in case of problems with e-mail. We patterned the mail protocol on Dillman's Tailored Design Method.[42]

Statistical Analysis

We pooled Internet and mail surveys for analyses because studies have revealed that physician attitudes are similar when obtained by different methods.[42–44] Physicians who did not deliver the HPV vaccine in their practice were excluded from analysis. We compared respondents with nonrespondents using t tests for continuous variables and Pearson's χ^2 tests for categorical variables. A multivariable analysis was conducted, with the outcome of reporting a $\geq$50% refusal or deferral of HPV vaccination rate among 11- to 12-year-old patients within each sex. We used a log-Poisson model with robust error estimation to calculate relative risks. Independent variables included physician and practice characteristics (specialty, number of providers in practice, proportion of adolescent patients, proportion of privately insured patients) and physician HPV vaccine recommendation style and delivery experiences. We used a cutoff of $P < .25$ for inclusion of variables into the model. We used a stepwise backward elimination procedure, in which the least significant predictor in the model was eliminated sequentially. At each step, estimates were checked to make sure other variables were not affected by dropping the least significant variable. This resulted in the retention of only those factors that were significant at $P < .05$ in the final model, with the exception of specialty, which we forced into the final model. All analyses were performed by using SAS version 9.4 (SAS Institute, Inc, Cary, NC).

RESULTS

The overall response rate was 65% (588 of 908); 70% (317 of 456) among pediatricians and 60% (271 of 452) among FPs. Of respondents, 280 (48%) responded via the Internet. Fifteen pediatricians and 43 FPs did not administer the HPV vaccine and were excluded. Reasons for not administering the HPV vaccine were not explored in this survey. In Table 1, we compare respondents and nonrespondents and show additional characteristics available only for respondents. Among FPs, respondents were significantly younger than nonrespondents and had more providers in their practices.

Delivery and Communication Practices for the HPV Vaccine

Within each specialty, a larger percentage of physicians made a strong recommendation for HPV vaccination for older adolescents compared with adolescents 11 to 12 years old (Fig 1). For each age group, a larger percentage of pediatricians than FPs made a strong recommendation. Sixty-five percent of pediatricians and 42% of FPs reported almost always or always using a presumptive style, whereas 16% of pediatricians and 24% of FPs almost always or always used a conversational style of introduction. Overall, 40% of physicians used standing orders for HPV vaccination, 66% had a computer-based system that could report adolescents who needed an HPV vaccine, and 42% had an electronic alert in the medical record if a patient needed an HPV vaccine (no significant differences by specialty).

Attitudes and Experiences With HPV Vaccine Delivery

A majority in both specialties strongly agreed or somewhat agreed that it is important that adolescents be vaccinated before they engage in physical intimacy (including kissing), that they encounter more resistance to HPV vaccination compared to other adolescent vaccines because it is not required by schools in their state, and that they encounter less resistance from patients and parents to beginning the HPV vaccine series at age 13 years than at age 11 years (Fig 2). Approximately one-third of physicians in both specialties reported anticipating an uncomfortable conversation if they recommended vaccination for patients at age 11 to 12 years.

Rates of Refusal or Deferral of the HPV Vaccine

Physicians reported high rates of refusal or deferral among 11- to 12-year-old patients, with lower levels among older adolescents (Fig 3); FPs reported higher rates than pediatricians at all patient ages, and physicians in both specialties were significantly more likely to report refusal or deferral for their male patients than for their female patients.

Factors significantly associated with physicians reporting a $\geq$50% refusal or deferral rate among 11- to 12-year-old patients included the following: not strongly recommending to 11- to 12-year-old patients, not almost always or always using a presumptive recommendation style, strongly agreeing that they encounter less resistance to HPV vaccination from patients age 13 years versus patients age 11 years, and anticipating an uncomfortable discussion when recommending to 11- to 12-year-old patients (Table 2). The multivariable results for both sexes were similar.

Perceived Barriers to HPV Vaccine Delivery

Perceived barriers to HPV vaccination that $\geq$20% of physicians in either specialty reported as major were the following: misinformation parents receive from the Internet or social media, parental concerns about the safety of the HPV vaccine, parents not

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TABLE 1 Respondent and Nonrespondent Characteristics by Physician Specialty

Characteristic	Pediatricians		FPs	
	Respondents (*n* = 317)	Nonrespondents (*n* = 139)	Respondents (*n* = 271)	Nonrespondents (*n* = 181)
Mean (SD)/median age, y	52 (10)/52	51 (11)/50	56 (8)/55*	58 (8)/58*
Mean (SD)/median No. providers	10 (16)/6	16 (55)/6	12 (35)/6**	7 (10)/5**
Male sex, %	36	34	59	60
Region, %				
Midwest	21	22	31	27
Northeast	23	15	16	16
South	35	44	30	36
West	21	19	24	20
Location of practice, %				
Rural	1	1	7	7
Urban (not inner city)	46	44	58	55
Urban (inner city)	53	56	35	38
Setting, %				
Private practice	80	78	70	76
University, hospital, public, or other	16	17	21	19
HMO	3	4	8	6
Decision-making				
Independent	72	65	51	60
Larger system level	28	35	49	40
Proportion of adolescents 11–18 y old in practice, %				
0%–9%	2	N/A	74	N/A
10%–19%	11	N/A	21	N/A
20%–29%	41	N/A	4	N/A
≥30%	46	N/A	2	N/A
Proportion of Hispanic patients in practice, %				
0%–9%	40	N/A	65	N/A
10%–24%	35	N/A	20	N/A
25%–49%	15	N/A	9	N/A
≥50%	11	N/A	6	N/A
Proportion of African American patients in practice, %				
0%–9%	44	N/A	72	N/A
10%–24%	33	N/A	19	N/A
25%–49%	18	N/A	6	N/A
≥50%	5	N/A	3	N/A
Proportion of patients with private insurance in practice, %				
0%–24%	24	N/A	33	N/A
25%–49%	22	N/A	21	N/A
50%–74%	28	N/A	29	N/A
75%–100%	25	N/A	26	N/A
Proportion of patients with Medicaid or CHIP in practice, %				
0%–9%	24	N/A	41	N/A
10%–24%	22	N/A	24	N/A
25%–49%	28	N/A	19	N/A
≥50%	25	N/A	16	N/A

CHIP, Children's Health Insurance Program; HMO, health maintenance organization; N/A, not applicable.

* $P < .05$ for *t* test for difference within specialty for respondents versus nonrespondents.

** $P < .05$ for Wilcoxon rank test for difference within specialty for respondents versus nonrespondents.

thinking the HPV vaccine was necessary for their daughters or sons, and opposition to vaccination for moral or religious reasons (Fig 4).

Knowledge, Practices, and Attitudes Regarding 2-Dose Schedules

Physicians, especially FPs, frequently were incorrect or reported not knowing about the number of doses recommended in different scenarios or whether additional vaccination with 9 valent HPV should be offered to adolescents who were fully immunized previously with 2 valent HPV or 4 valent HPV (Fig 5). Regarding dosing intervals, among pediatricians, 74% reported routinely recommending the second HPV dose 6 months after the first, and 25% reported routinely recommending it at 12 months; among FPs, corresponding percentages were 88% at 6 months and 12% at a 12 months ($P < .0001$).

The vast majority of physicians strongly or somewhat agreed that the 2-dose schedule is as efficacious as a 3-dose schedule for adolescents <15 years and that the new schedule facilitated completion and initiation of the series among adolescents in this age group, with pediatricians being more likely to strongly agree with all of these statements than FPs (Fig 6). However, more than half of FPs and close to one-third of pediatricians strongly or somewhat agreed that having different recommendations for adolescents ≥15 years old and younger adolescents created confusion among patients and parents or practice staff.

DISCUSSION

Despite the existence of highly effective and safe HPV vaccines, national vaccination coverage remains suboptimal. This is the first national survey of physician attitudes regarding the new ACIP recommendations for a 2-dose schedule in younger adolescents, and it offers a glimpse into physician

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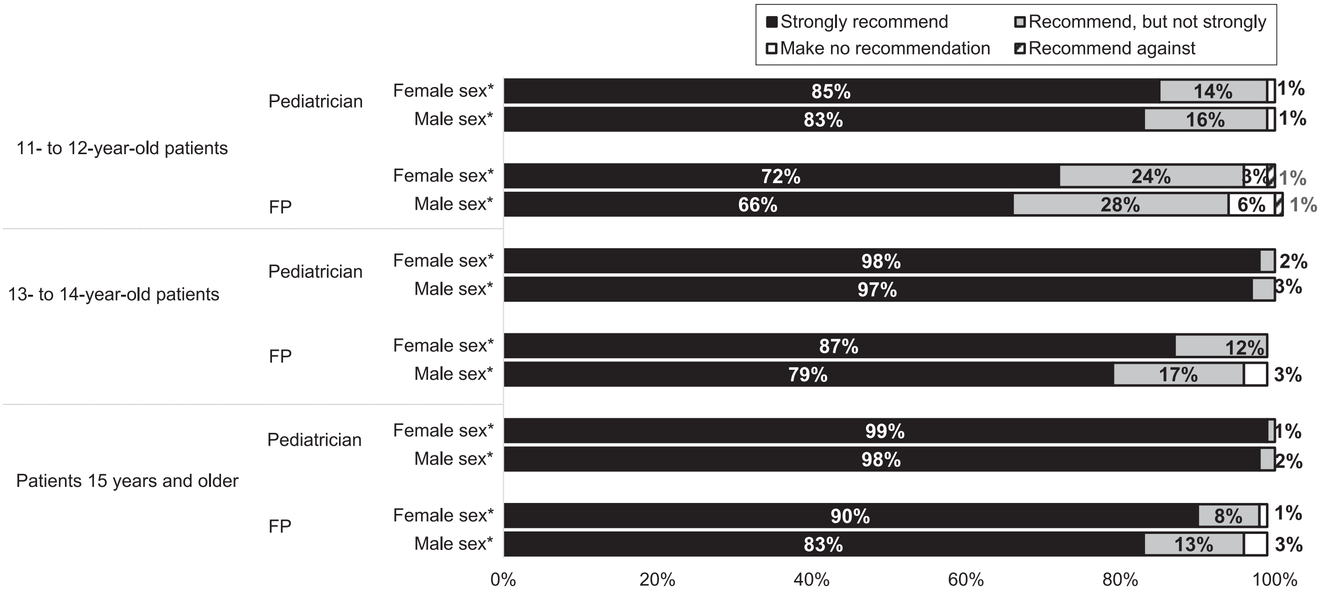

FIGURE 1

Strength of physician recommendation for HPV vaccine by patient age and sex (pediatricians, *n* = 302; FPs, *n* = 228). All comparisons between male and female patients within each age group within specialty differ significantly at $P < .05$ (Fisher's exact test). * $P < .05$ for comparison between FPs and pediatricians (Fisher's exact test).

practices with respect to current HPV vaccine recommendations and delivery practices. Our data reveal that a high proportion of physicians are recommending the HPV vaccine, although more are recommending it for older adolescents than for those 11 to 12 years old. A lower proportion of FPs compared with pediatricians strongly recommend the HPV vaccine to patients of all ages evaluated. Slightly more than half of pediatricians and less than half of FPs reported using a presumptive recommendation style, and less than half of those in both specialties used standing orders or electronic alerts in HPV vaccine delivery. Physicians reported high rates of refusal, especially by 11- to 12-year-old patients, who are the target population for vaccination according to national guidelines. Physicians were more likely to report high refusal rates by 11- to 12-year-old patients if physicians did not use a presumptive style, if physicians did not strongly recommend vaccination to young adolescents, or if physicians anticipated less resistance to vaccination from patients older than 11 or 12 years. Although physicians demonstrated some knowledge gaps about the 2-dose recommendations, the majority believed that the revised schedule was facilitating both initiation and completion of the HPV vaccine series among adolescents <15 years of age.

A physician recommendation has been shown to be 1 of the most important factors in parental vaccine acceptance,[27–29] and the lack of a strong recommendation has been identified as an important barrier to HPV vaccination.[22,45–48] Our data reveal substantial increases in the strength of recommendation when compared with a survey conducted ~5 years ago by using similar methodology.[49] Percentages of pediatricians strongly recommending the HPV vaccine have increased from 60% in the 2013 survey to 85% in the 2018 survey for 11- to 12-year-old girls and from 52% to 83% for 11- to 12-year-old boys. Smaller increases have occurred among FPs during the same period (from 59% to 72% for 11- to 12-year-old girls and from 41% to 66% for 11- to 12-year-old boys), although the disparity in strength of recommendations between specialties persists.[49] Although the overall percentage of physicians who strongly recommended the HPV vaccine for patients age 11 to 12 years was high in the current study, it was 13 to 15 absolute percentage points lower than that for patients age 13 to 14 years old in both specialties.

Lower rates of strong recommendations for HPV vaccination among FPs have important implications given their prominent role in adolescent health care delivery. A recent national analysis revealed that the proportion of adolescents seen by FPs increases from 25% among 11-year-old male patients to 57% among 18-year-old male patients and from 31% among 11-year-old female patients to 41% among 18-year-old female patients.[50] The differences we observed by specialty are reflective of previous literature regarding childhood[51–56] and adolescent[49,57–62] vaccines and highlight the fact that FPs need to remain a major focus of vaccine

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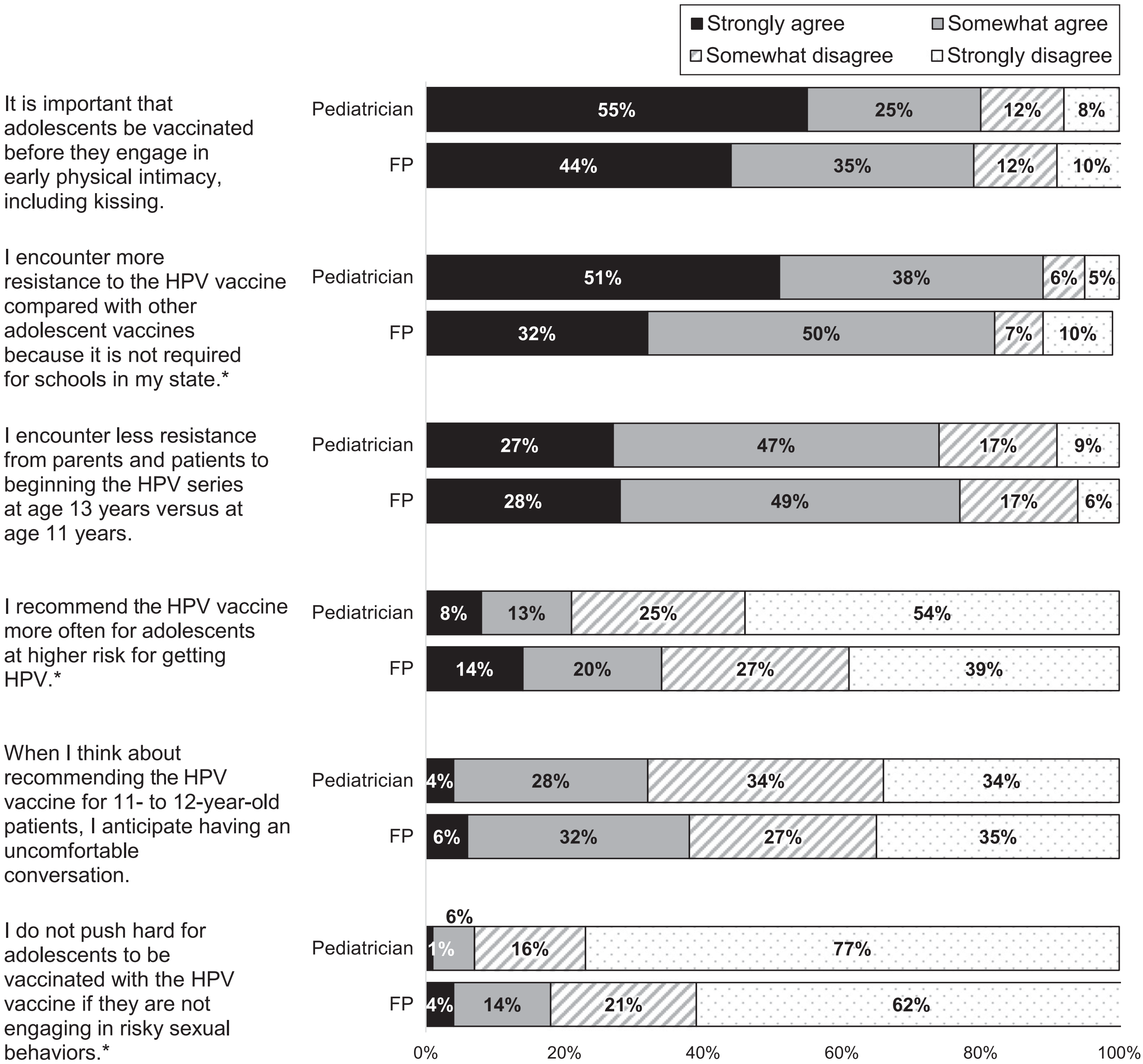

FIGURE 2

Physician experiences with HPV vaccine discussions (pediatricians: $n = 302$; FPs: $n = 228$). * $P < .05$ for comparison between FPs and pediatricians (χ^2 test). Some percentage do not add up to 100% because of rounding.

education and practice improvement strategies to improve HPV vaccine delivery.

Reported rates of deferrals or refusals were high among our respondents, especially for patients ages 11 to 12 years and among FPs and appear relatively stable from 5 years ago.[49] Physicians, especially FPs, reported higher rates of deferral or refusal for their male patients compared with female patients in every age group. This may be related to the longer duration of recommendations for female patients or to a higher perceived benefit of the HPV vaccine for female patients. Physicians who perceive higher refusal or deferral rates among 11- to 12-year-old patients more frequently were those who (1) did not strongly recommend vaccination in this age group, (2) anticipated uncomfortable discussions with parents of 11- to 12-year-old patients, and (3) expected to encounter more resistance from parents of 11- to 12-year-old patients versus older adolescents. This finding is consistent with those of previous studies demonstrating that physicians are less likely to discuss the HPV vaccine with patients aged 11 to 12 years if they believe parents are likely to defer.[49,63,64] However, other literature has revealed that

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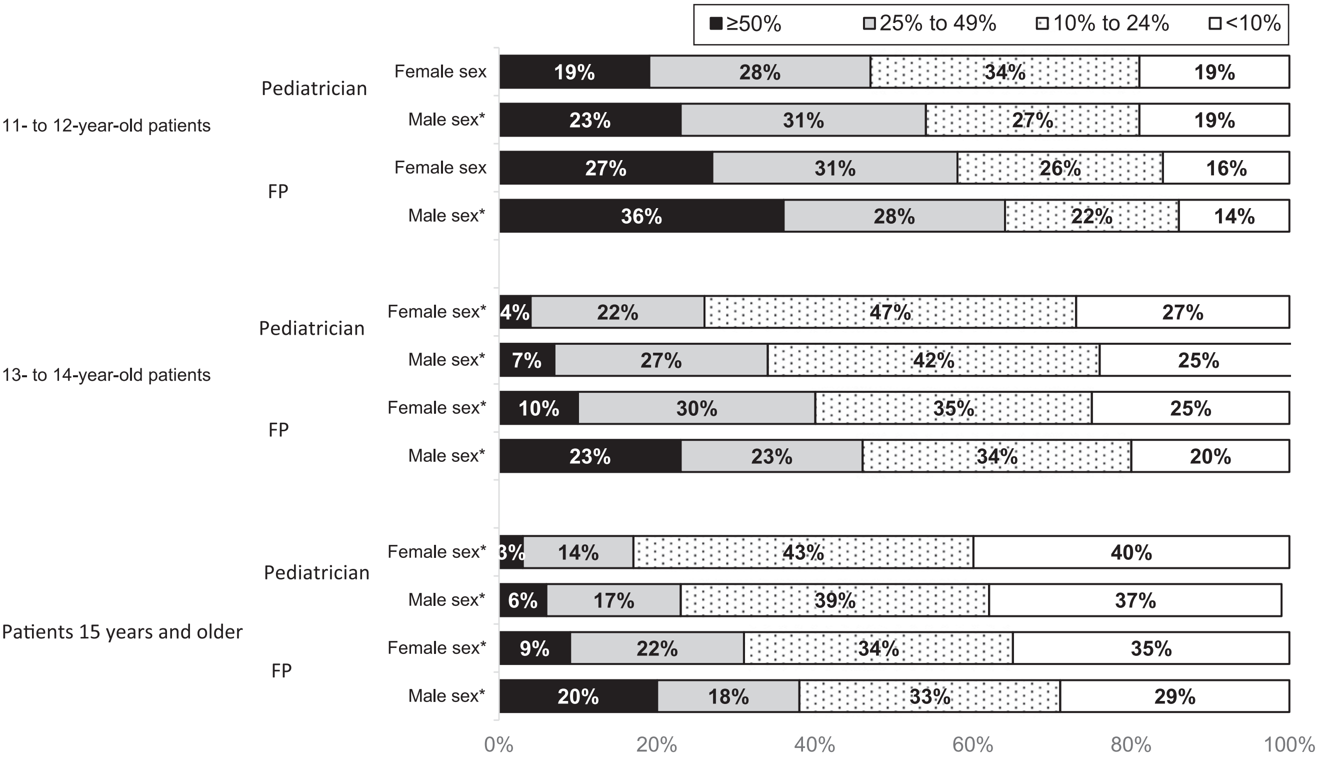

FIGURE 3

Proportion of physicians reporting patients and/or parents refusal or deferral of the HPV vaccine, by patient age and sex (pediatricians: $n = 302$; FPs: $n = 228$). All comparisons between male and female patients within each age group within specialty differ significantly at $P < .05$ (χ^2 test). Some bars do not add up to 100% because of rounding. * $P < .05$ for comparison between FPs and pediatricians (χ^2 test).

physicians may considerably overestimate the amount of resistance to vaccination that they are likely to encounter.[65] Our data also reveal that physicians who report high levels of refusal or deferral are also less likely to use a presumptive recommendation style. To our knowledge, this has not previously been reported. The circular nature of provider anticipation of refusal or deferral potentially leading to a weaker recommendation style and less persistence in responding to parental hesitancy[66] could be creating a self-perpetuating cycle within a subgroup of physicians.

Our data suggest that improvements are needed in how the HPV vaccine is being recommended. A presumptive[41] style of initiating HPV vaccine discussions uses words that convey an assumption of vaccination and does not discuss the HPV vaccine in a different manner than other adolescent vaccines, whereas, a conversational[30] style engages parents in an open-ended discussion about the HPV vaccine without linguistic presupposition of vaccination. A presumptive approach has been shown to be associated with higher HPV acceptance compared with a conversational approach in multiple studies.[30–33] Updated implementation guidance from the AAP includes the use of a strong pediatrician recommendation with wording consistent with a presumptive style,[39] and the AAFP Web site refers FPs to Centers for Disease Control and Prevention talking points that included recommendations for "same way" as for other adolescent vaccines and "same day" recommendations. Our data indicate that large percentages of physicians, including a majority of pediatricians, have adopted the presumptive communication style in initiating HPV vaccine discussion, but there are still substantial proportions who have not. In addition to improving physician communication styles, HPV vaccine delivery could also be optimized by increased use of evidence-based methods, including standing orders and alert systems in the medical record to remind providers of the need for vaccination at the point of care, both of which are recommended by the Community Preventive Services Task Force.[67,68]

Factors reported by physicians as important barriers to HPV vaccination (including perceived parental concerns about safety or effects of vaccination on sexual behavior and parents thinking that the HPV vaccine is not necessary or that there are too many vaccines at 1 visit) are consistent with previously identified barriers.[22] However, the barrier most frequently reported by physicians in both specialties (the effect of misinformation parents

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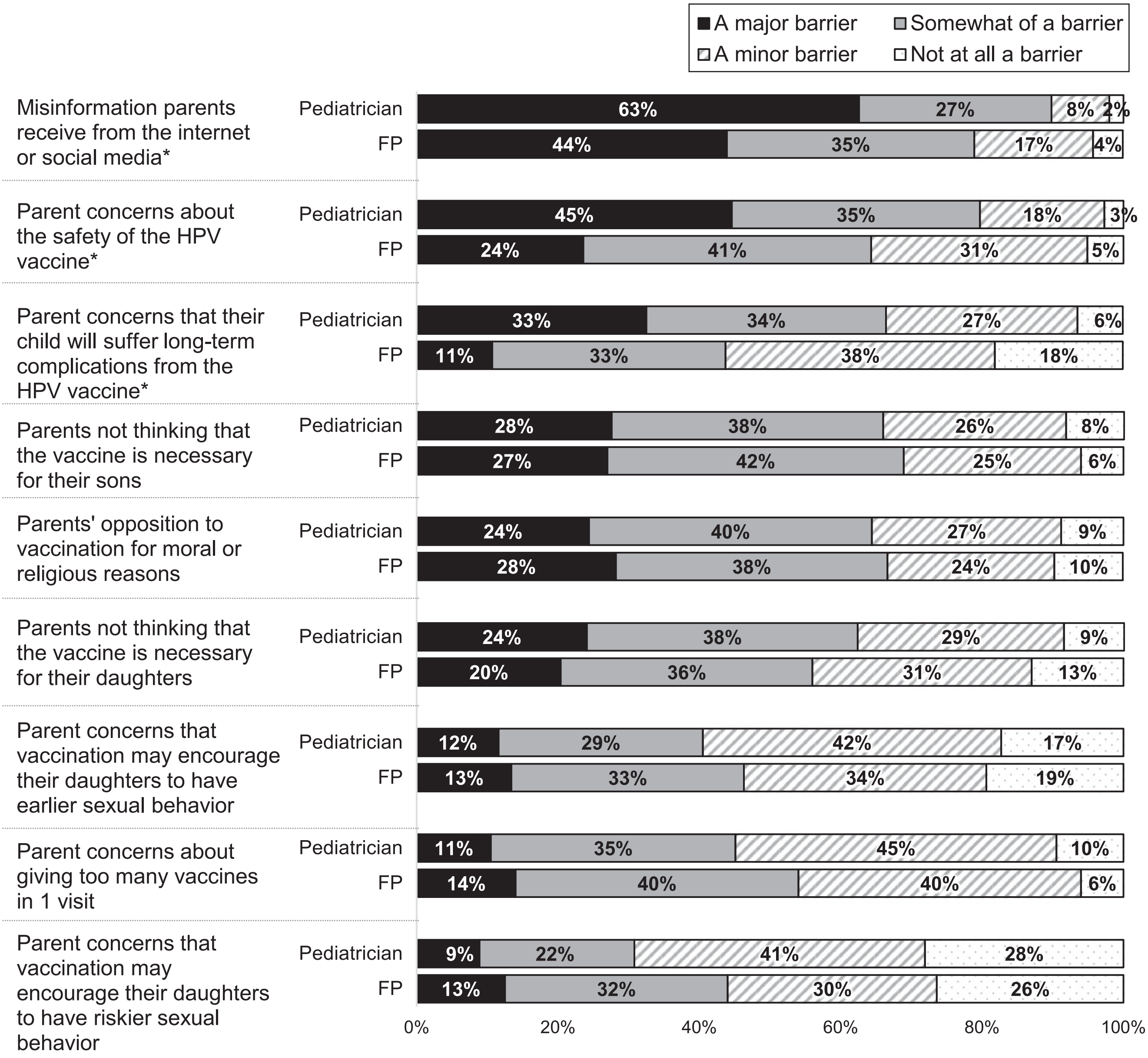

FIGURE 4

Physicians perceived barriers to HPV vaccination (pediatricians: $n = 302$; FPs: $n = 228$). Some bars do not add up to 100% because of rounding. Barriers reported as major by $<12\%$ by both specialties include the following: parent concerns that vaccination may encourage their sons to have earlier sexual behavior, that vaccination may encourage their sons to have riskier sexual behavior, that the vaccine could cause infertility in their daughters and/or sons, or that their child will suffer immediate short-term effects from the HPV vaccine; parent concerns about the efficacy of the HPV vaccine and about waning immunity if the HPV vaccine is given too early; physician concern about giving too many vaccines in 1 visit (it will result in an uncomfortable conversation with the parent), about the safety of the HPV vaccine for female patients, and about the efficacy of the HPV vaccine for male and female patients; physician belief that HPV infection is not common enough in male and female patients to justify a vaccination, that Papanicolaou tests are an adequate way to prevent cervical cancer, and that HPV-associated diseases are not severe enough in male and female patients to justify a vaccination; parents wanting to wait to begin the HPV series until after menarche for girls; failure of some insurance companies to cover HPV vaccination; the up-front costs for a practice to purchase the vaccine; lack of adequate reimbursement for vaccination; and the time it will take a physician to discuss HPV vaccination with his or her patients and their parents. * $P < .05$ for comparison between FPs and pediatricians (χ^2 test).

receive from the Internet or social media) is one that has not been frequently highlighted. Although social media have been recognized as a significant source of vaccine-critical content,[69–72] its contribution to low HPV vaccination acceptance has not been well studied. A recent survey of 1263 parents of US adolescents revealed that stories of HPV vaccine harms were more commonly found in social media than in traditional media or conversations and were associated with lack of initiation, delay, or refusal of HPV vaccination.[73] Along

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TABLE 2 Characteristics of Physicians Reporting a 50% or Higher Refusal or Deferral Rate for HPV Vaccination Among Their 11- to 12-Year-Old Patients by Sex

	Female Patients (*n* = 482)			Male Patients (*n* = 497)		
	<50% Refusal or Deferral Rate (*n* = 376; 78%)	≥50% Refusal or Deferral Rate (*n* = 106; 22%)	MV RR (95% CI)	<50% Refusal or Deferral Rate (*n* = 356; 72%)	≥50% Refusal or Deferral Rate (*n* = 141; 28%)	MV RR (95% CI)
Physician and practice characteristics						
Practice specialty						
FP	39%	50%	1.11 (0.81–1.52)	38%	54%	1.30 (0.99–1.69)
Pediatrician	61%	50%	Reference	62%	46%	Reference
No. providers in practice, median (IQR)	6 (4–11)	5 (3–9)	N/A	6 (4–11)	5 (3–10)	N/A
Proportion of adolescents 11–18 y old in practice, %						
0%–9%	20	31	[a]	21	29	[a]
≥10%	80	69	N/A	79	71	N/A
Proportion of patients with private insurance in practice, %						
0%–24%	26	16	[a]	25	22	[a]
≥25%	74	84	N/A	75	78	N/A
HPV recommendation style						
Strongly recommend to adolescents 11–12 y old						
Yes	88%	51%	Reference	86%	52%	Reference
No	12%	49%	2.14 (1.50–3.04)	14%	48%	1.90 (1.43–2.53)
Use of a presumptive recommendation style						
Frequently, occasionally, rarely, or never	36%	66%	1.61 (1.11–2.32)	34%	67%	1.74 (1.27–2.38)
Almost always or always	64%	34%	Reference	66%	33%	Reference
Delivery experiences and attitudes						
Perceive less resistance from parents and patients to beginning the HPV series at age 13 y versus at age 11 y						
Strongly agree	20%	54%	2.33 (1.69–3.22)	20%	47%	1.84 (1.42–2.38)
Other	80%	46%	Reference	80%	53%	Reference
Do not push hard for adolescents to be vaccinated with HPV vaccine if they are not engaging in risky sexual behaviors, %			[a]			[a]
Strongly or somewhat agree	8	23	N/A	8	20	N/A
Strongly or somewhat disagree	92	77	N/A	92	80	N/A
Anticipate having an uncomfortable conversation when recommending HPV vaccine for adolescents 11–12 y old						
Strongly or somewhat agree	30%	51%	1.62 (1.17–2.24)	30%	46%	1.32 (1.02–1.72)
Strongly or somewhat disagree	70%	49%	Reference	70%	54%	Reference

CI, confidence interval; IQR, interquartile range; MV, multivariable regression; RR, relative risk; N/A, not applicable.

[a] Variables were not significant in the multivariable model and were therefore excluded from the final model.

with these data, our findings highlight the importance of developing effective public health communication strategies to counter misinformation and highlight benefits of HPV vaccination via social media.

Given the relative recency of recommendations for the 2-dose schedule for adolescents initiating HPV vaccination before age 15 years, it is not surprising that there were knowledge gaps for proportions of physicians about when a third dose is recommended, the acceptability of using different HPV vaccines to complete the series, and the need for an additional 9 valent HPV vaccination in those already fully vaccinated with either 2 valent HPV or 4 valent HPV. Physician knowledge should increase over time, as will, presumably, the ability of the electronic medical record or immunization registry–based systems to forecast the need for HPV vaccination. Interestingly, the majority of physicians in both specialties reported recommending the second dose of the 2-dose schedule at a 6-month interval rather than 12 months later at the next annual well-child visit,

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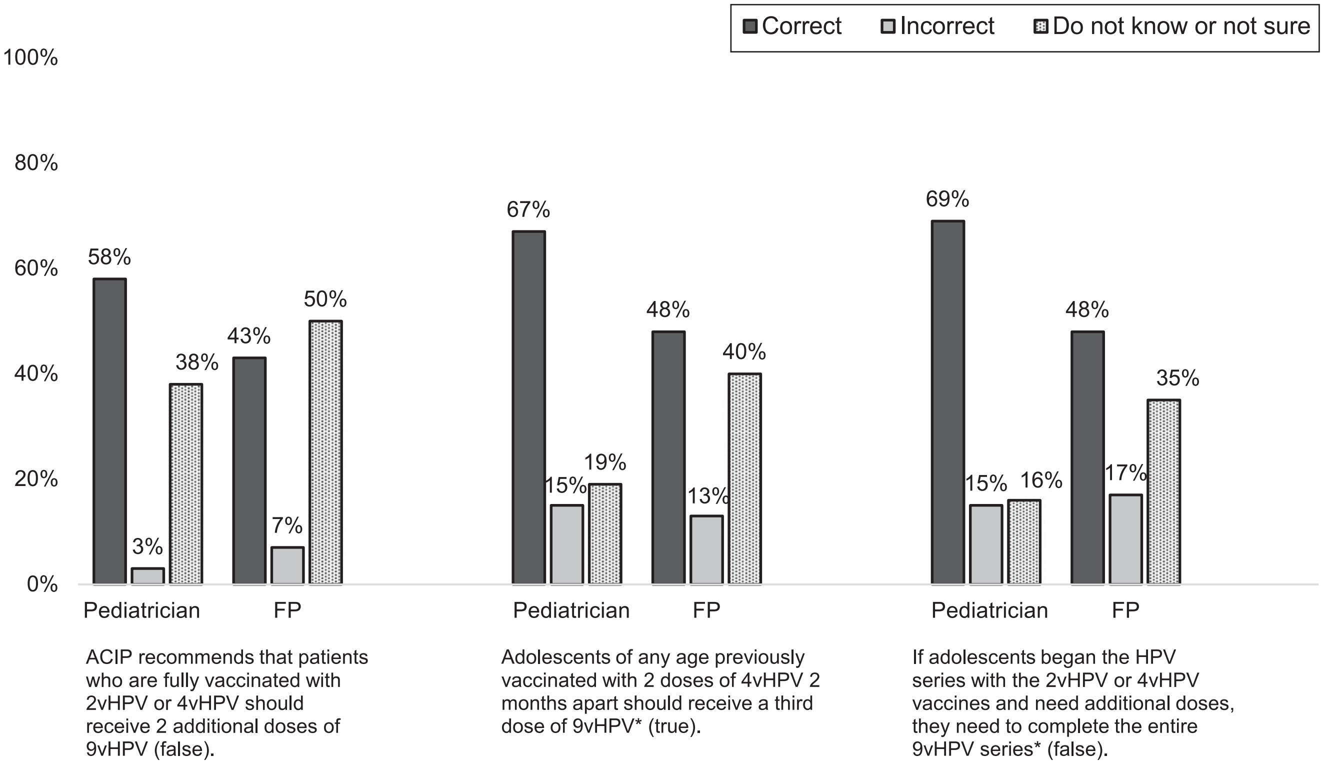

FIGURE 5

Physician knowledge regarding 2-dose HPV vaccine schedules (pediatricians: n = 302; FPs: n = 228). * $P < .05$ for comparison between FPs and pediatricians (χ^2 test). 2vHPV, 2 valent HPV; 4vHPV, 4 valent HPV; 9vHPV, 9 valent HPV.

although national guidelines allow for either. This may reflect an understanding of the importance of series completion as soon as possible. Importantly, primary care physicians strongly endorsed the belief that the 2-dose schedule was facilitating both initiation and completion of the HPV series.

There are important strengths and limitations to our data. We surveyed large, nationally representative samples of pediatricians and FPs and achieved high response rates. Responses of our sentinel physicians may not be fully generalizable, although previous work has revealed that the survey methods described yield similar responses to the most commonly employed method of sampling physicians nationally.[24] Nonrespondents might have different views than respondents, although our high response rates helps to mitigate against this source of bias. Most importantly, our data are based on self-report rather than direct observation and may not entirely reflect actual physician practice.

This snapshot of HPV vaccine delivery in primary care demonstrates room for improvement in the way physicians are communicating about the HPV vaccine and in their delivery practices. Most important in this regard is the continued finding that physicians who experience or expect to experience high rates of deferral or refusal may be anticipating and accommodating refusals by altering their recommendation strength and style. Such accommodations by physicians may perpetuate a lack of acceptance of the HPV vaccine among parents. Greater physician awareness about the potential of overestimating the degree of parental resistance to HPV vaccination and about the effectiveness of a strong recommendation for the HPV vaccine, delivered in the same way as for other adolescent vaccines and on same day as other adolescent vaccines, may be key to increasing acceptance among parents of 11- to 12-year-old patients. Increased use of available communication training materials and applications as well as further development of evidence-based messages for parents may be helpful in improving the way HPV vaccination is introduced.[74–78] Our data are encouraging in revealing substantial increases over the past 5 years in the percentage of physicians who report strongly recommending the HPV vaccine to 11- to 12-year-old patients. The findings also reveal that according to primary care physicians, the 2-dose schedule could result in meaningful

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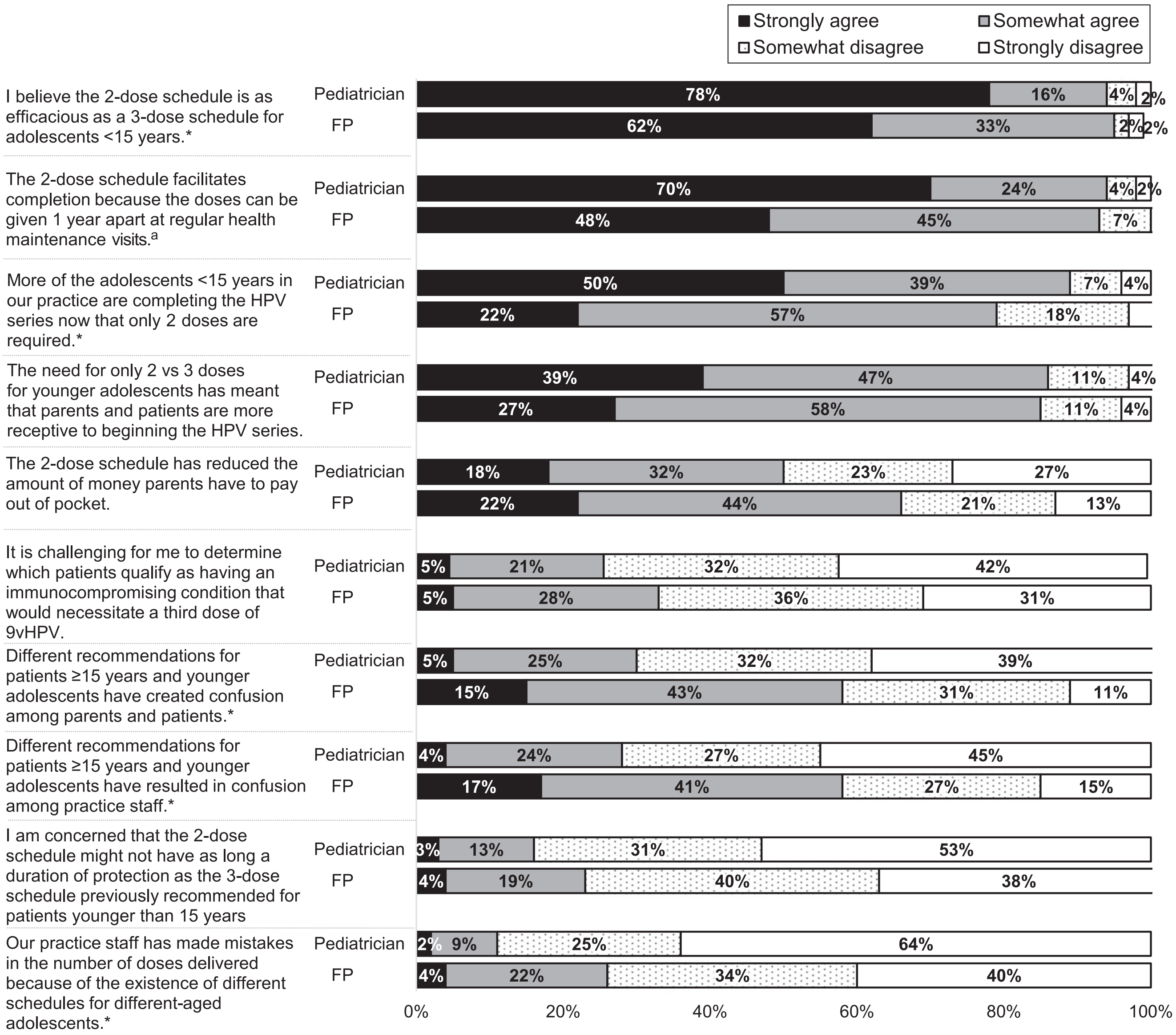

FIGURE 6

Primary care physicians' attitudes regarding the 2-dose HPV vaccine (pediatricians: $n = 302$; FPs: $n = 228$). Some bars do not add up to 100% because of rounding. [a] Fisher's exact test.* $P < .05$ for comparison between FPs and pediatricians (χ^2 test). 9vHPV, 9 valent HPV.

increases in HPV vaccination initiation and completion among adolescents, leading to greater protection against HPV-associated cancers in the United States.

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ABBREVIATIONS

AAFP: American Academy of Family Physicians
AAP: American Academy of Pediatrics
ACIP: Advisory Committee on Immunization Practices
FP: family physician
HPV: human papillomavirus

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and reviewed and revised the manuscript; Dr Brtnikova contributed to the study design and data collection instrument design, coordinated and supervised all data collection, and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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HPV Vaccine Delivery Practices by Primary Care Physicians

Allison Kempe, Sean T. O'Leary, Lauri E. Markowitz, Lori A. Crane, Laura P. Hurley, Michaela Brtnikova, Brenda L. Beaty, Elissa Meites, Shannon Stokley and Megan C. Lindley

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Parenteral Antibiotic Therapy Duration in Young Infants With Bacteremic Urinary Tract Infections

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abstract

OBJECTIVES: To determine the association between parenteral antibiotic duration and outcomes in infants ≤60 days old with bacteremic urinary tract infection (UTI).

METHODS: This multicenter retrospective cohort study included infants ≤60 days old who had concomitant growth of a pathogen in blood and urine cultures at 11 children's hospitals between 2011 and 2016. Short-course parenteral antibiotic duration was defined as ≤7 days, and long-course parenteral antibiotic duration was defined as >7 days. Propensity scores, calculated using patient characteristics, were used to determine the likelihood of receiving long-course parenteral antibiotics. We conducted inverse probability weighting to achieve covariate balance and applied marginal structural models to the weighted population to examine the association between parenteral antibiotic duration and outcomes (30-day UTI recurrence, 30-day all-cause reutilization, and length of stay).

RESULTS: Among 115 infants with bacteremic UTI, 58 (50%) infants received short-course parenteral antibiotics. Infants who received long-course parenteral antibiotics were more likely to be ill appearing and have growth of a non–*Escherichia coli* organism. There was no difference in adjusted 30-day UTI recurrence between the long- and short-course groups (adjusted risk difference: 3%; 95% confidence interval: −5.8 to 12.7) or 30-day all-cause reutilization (risk difference: 3%; 95% confidence interval: −14.5 to 20.6).

CONCLUSIONS: Young infants with bacteremic UTI who received ≤7 days of parenteral antibiotics did not have more frequent recurrent UTIs or hospital reutilization compared with infants who received long-course therapy. Short-course parenteral therapy with early conversion to oral antibiotics may be considered in this population.

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WHAT'S KNOWN ON THIS SUBJECT: Infants ≤60 days old with bacteremic urinary tract infection often receive prolonged courses of parenteral antibiotics. The safety of short-course parenteral antibiotic therapy has not been established in this population.

WHAT THIS STUDY ADDS: In this multicenter study of infants ≤60 days old with bacteremic urinary tract infection, infants receiving ≤7 days of parenteral antibiotics did not experience more frequent UTI recurrence or hospital reutilization compared with infants receiving >7 days of parenteral therapy.

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Urinary tract infection (UTI) is 1 of the most common bacterial infections in infants ≤60 days of age.[1–3] Approximately 8% to 10% of young infants with UTI have concomitant bacteremia.[2,4,5] However, no evidence-based guidelines exist to direct management in this population, particularly regarding optimal parenteral (ie, intravenous and/or intramuscular [IV/IM]) antibiotic duration.

Although several studies have supported the safety of short-course parenteral antibiotic therapy with early conversion to oral antibiotics in young infants with uncomplicated UTI,[6–8] the safety of short-course parenteral antibiotic therapy in young infants with bacteremic UTI has not been established. As a result, infants with bacteremic UTI often receive prolonged courses of parenteral antibiotics, which can lead to long hospitalizations and increased costs. Furthermore, the peripherally inserted central catheters (PICCs) often required to deliver prolonged parenteral antibiotic therapy expose infants to added risks, including catheter-associated bloodstream infections as well as mechanical and thrombotic central-line complications.[9,10] The benefit of prolonged parenteral antibiotic therapy is unclear in this population.[6,8,11]

Our objective for this study was to examine the association between parenteral antibiotic duration and clinical outcomes in infants ≤60 days old with bacteremic UTI.

METHODS

Study Design

This study was nested within a multicenter retrospective cohort study[12,13] of young infants evaluated for invasive bacterial infections in the emergency departments (EDs) of 11 geographically diverse children's hospitals (Supplemental Table 3). The study was approved by each site's institutional review board with a waiver of informed consent and permission for data sharing.

Study Population

Infants ≤60 days old who presented to the EDs of the 11 participating hospitals between July 1, 2011, and June 30, 2016, were included in the parent study if they had a bacterial pathogen isolated in blood or cerebrospinal fluid (CSF) culture. Pathogenic bacteria were determined a priori via literature review and expert consensus (Supplemental Table 4).[12,13] For this substudy, we included infants from the parent study who were diagnosed with a UTI and had detection of the same bacterial pathogen in both blood and urine cultures (Fig 1). UTI was defined as growth of ≥50 000 colony-forming units (CFUs)/mL of a pathogen in urine culture or growth of ≥10 000 CFUs/mL of a pathogen in urine culture plus an abnormal urinalysis (defined as presence of leukocyte esterase, nitrites, or >5 white blood cells per high-power field on urine microscopy).[4,14,15] We excluded infants who had a bag or unknown collection method for urine culture if pathogen growth was <100 000 CFUs/mL or if multiple organisms were isolated because these organisms could represent contaminants.[16,17] Infants who had concomitant bacterial meningitis, infants with CSF pleocytosis who received antibiotic pretreatment, and infants with examination and laboratory findings consistent with focal infections, such as septic arthritis, were also excluded from our cohort because these infants would likely be prescribed prolonged courses of parenteral antibiotics for treatment of other invasive infections. Finally, we excluded infants who died and those who were transferred out from the participating institution before completion of parenteral antibiotic therapy because we could not report total duration of IV/IM antibiotic therapy in these patients.

Data Sources

Each site's electronic medical record system or microbiology laboratory was queried to identify all infants who had a positive blood or CSF culture result collected in the ED during the study period. A medical record review was then conducted to confirm eligibility. Information on patient demographics, clinical variables (eg, presence of fever and physical examination findings), laboratory data, parenteral antibiotic duration, adverse events, and 30-day ED revisit or readmission were also obtained via detailed medical record review.

Exposure

The exposure of interest was duration of parenteral antibiotic therapy. Patients were divided into short-course and long-course exposure groups. Given that we found a somewhat bimodal distribution of parenteral antibiotic duration with a median duration of 7 days (Supplemental Fig 2), we defined short course as receipt of parenteral antibiotics for ≤7 days and long course as receipt of parenteral antibiotics for >7 days.

Outcomes

The primary outcome was recurrence of UTI that resulted in an ED revisit or hospitalization within 30 days of discharge from the index hospital admission. For infants who had recurrent UTI, we conducted additional medical record review to obtain information on timing of recurrence, causative organism at recurrence, presence of bacteremia or meningitis at recurrence, diagnosis of vesicoureteral reflux (VUR), and use of prophylactic antibiotics before recurrence. Secondary outcomes included hospital length of stay (LOS), 30-day all-cause reutilization (defined as hospital readmission or ED revisit within 30 days of index discharge),

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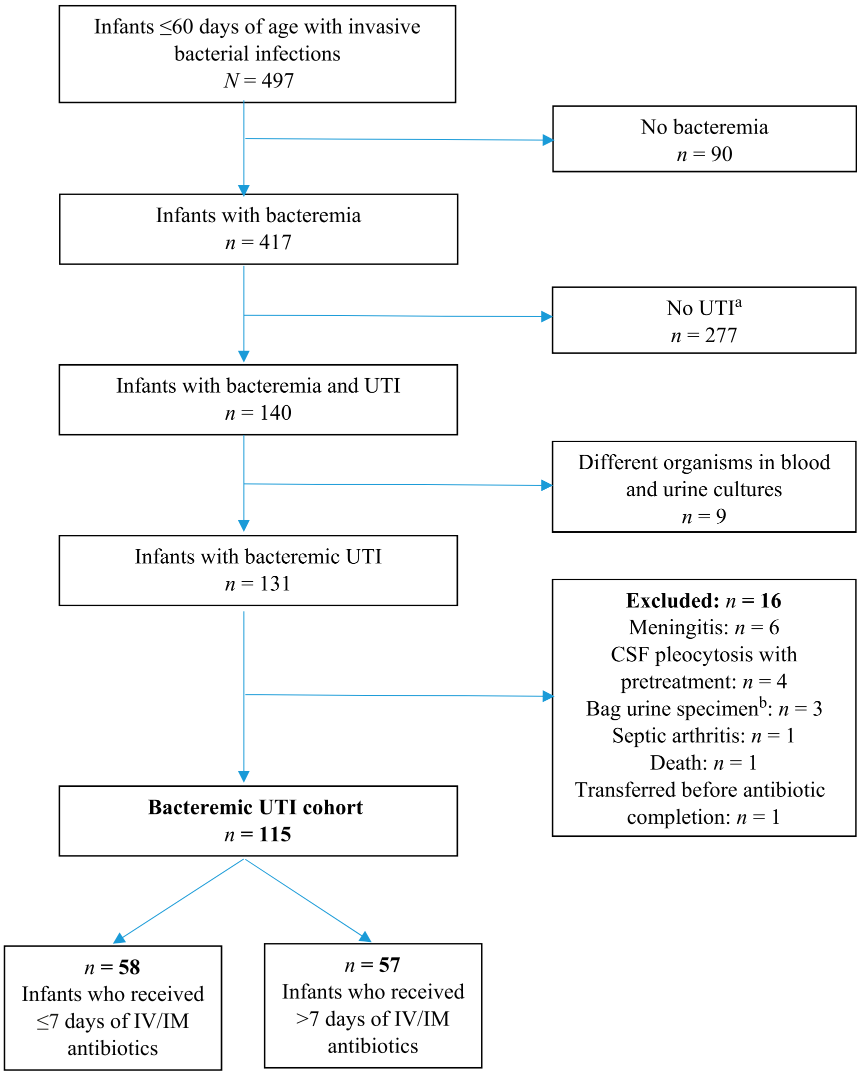
Infants ≤60 days of age with invasive bacterial infections
N = 497
No bacteremia
n = 90
Infants with bacteremia
n = 417
No UTI[a]
n = 277
Infants with bacteremia and UTI
n = 140
Different organisms in blood and urine cultures
n = 9
Infants with bacteremic UTI
n = 131
Excluded: n = 16
Meningitis: n = 6
CSF pleocytosis with pretreatment: n = 4
Bag urine specimen[b]: n = 3
Septic arthritis: n = 1
Death: n = 1
Transferred before antibiotic completion: n = 1
Bacteremic UTI cohort
n = 115
n = 58
Infants who received ≤7 days of IV/IM antibiotics
n = 57
Infants who received >7 days of IV/IM antibiotics

FIGURE 1

Flowchart of the study population. [a] UTI definition: positive urine culture result with ≥50 000 CFUs/mL or ≥10 000 CFUs/mL with an abnormal urinalysis (leukocyte esterase-positive or nitrite-positive or >5 WBCs). [b] Patients who had a bag or unknown method of urine culture collection were excluded if the culture grew <100 000 CFUs/mL or if >1 organism was isolated. WBC, white blood cell.

and adverse events within 30 days of discharge (ie, readmission to an ICU, need for mechanical ventilation or vasopressor use, or neurologic sequelae).

Covariates

Covariates of interest included patient age, sex, prematurity (defined as gestational age <37 weeks), complex chronic condition,[18] known genitourinary anomaly, presence of fever (ie, a reported temperature ≥38.0°C (100.4°F) at home, in an outpatient clinic, or documented in the ED and obtained via any method), ill appearance, ICU stay during the index admission, causative pathogen, and prolonged bacteremia. Ill appearance was defined as any of the following physical examination terms documented on arrival to the ED: "ill appearing," "toxic," "limp," "unresponsive," "gray," "cyanotic," "apnea," "weak cry," "poorly perfused," "grunting," "listless," "lethargic," or "irritable."[19] If none of these terms were documented, the infant was classified as not ill appearing. In cases of contradicting documentation of ill appearance between attending physician and trainee, the attending physician's documentation was used. Prolonged bacteremia was defined as isolation of the initial pathogen on a repeat blood culture drawn at least 24 hours after the initial culture.[20]

Statistical Analysis

Categorical variables were described by using frequencies and percentages. To adjust for potential confounding by indication for duration of parenteral antibiotic therapy, we generated a propensity score for each patient to estimate the conditional probability of receiving long-course parenteral antibiotic therapy.[21,22] Propensity scores were calculated by using a multivariable logistic regression model that consisted of baseline demographic characteristics (ie, age and sex), past medical history (ie, prematurity, presence of chronic complex condition, and known genitourinary anomaly), and clinical characteristics at presentation (ie, fever, ill appearance, ICU stay, prolonged bacteremia, and causative organism).

We then conducted inverse probability weighting (IPW), aiming to achieve balance in the distribution of covariates between exposure groups by multiplying each study observation by the inverse of its respective propensity score to achieve a statistically balanced pseudo-study population.[21] Distributional balance of covariates between short-course and long-course antibiotic groups after the weighting procedure was examined by using standardized mean differences, with the magnitude of ≤0.1 indicating acceptable balance (Supplemental Table 5).[21] One variable, prolonged bacteremia, remained unbalanced; however, it was neither significantly associated with the outcomes of recurrent UTI and reutilization, as tested by Fisher's

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exact test, nor with LOS, as tested by the Wilcoxon rank test. To incorporate the effect of study site, we attempted 2 additional models to generate propensity scores: 1 in which study site was used as a fixed-effect predictor in the above logistic regression and a second in which a random intercept was added for each study site. However, neither model yielded adequate balance between covariates. Thus, the multivariable logistic regression model without study site (Supplemental Table 5) was used for the analysis.

To evaluate the association of antibiotic duration with our outcomes of interest, we employed marginal structural models and applied them to our weighted population.[23] We used the logit link function to estimate the probability of recurrent UTI and reutilization in each group and summarized our findings using both relative risk and risk difference. We used the identity link to estimate the adjusted difference in the mean LOS between short-course and long-course treatment groups. Natural log transformation was applied to LOS before its modeling in the marginal structural models. Statistical significance was established at the 2-sided α level of .05. Data were analyzed by using R version 3.4.3 statistical software[24] and by using the following statistical packages: lme4,[25] tableone,[26] ipw,[27] sandwich,[28] and survey.[29]

RESULTS

Patient Characteristics

Of the 497 infants ≤60 days old in the parent study cohort who had a pathogen isolated in blood or CSF culture, we identified 140 infants with bacteremia and UTI caused by the same pathogen. Applying exclusion criteria, we assembled a cohort of 115 infants ≤60 days of age with bacteremic UTI (Fig 1). Of this cohort, 52% of infants were ≤28 days of age, 60% were boys, and 9% were premature (Table 1). A subset of patients had a complex chronic condition or known genitourinary anomaly on admission, and the majority of infants presented with fever (Table 1).

Urine culture was obtained via catheterization for 110 (96%) infants in our cohort. *Escherichia coli* was the most common causative organism and was found in 93 infants (81%). Six infants (5%) grew *Enterococcus faecalis*, 5 (4%) grew *Staphylococcus aureus*, 4 (3%) grew *Klebsiella* spp, 3 (3%) infants grew *Streptococcus agalactiae*, 3 (3%) grew *Enterobacter* spp, and 1 (1%) grew *Citrobacter* spp from blood and urine cultures. Of note, all 5 infants with *S aureus* bacteremia were eventually diagnosed with urinary tract anomalies.

We included a total of 5 patients growing >100 000 CFUs/mL of *E coli* in a bagged urine specimen. Of these, 4 had evidence of pyuria, and 1 patient did not have a urinalysis conducted. All patients grew *E coli* in the blood with identical antibiotic susceptibilities.

Eight infants (7%) had prolonged bacteremia; all 8 patients with prolonged bacteremia in our cohort grew organisms that were sensitive to the empirical antibiotics they had been receiving since admission. No patients grew extended-spectrum β-lactamase–producing organisms in a blood or urine culture. All pathogens identified in our cohort were susceptible to an antibiotic with an available oral alternative.

The median duration of parenteral antibiotic therapy was 7 days (range: 2–24 days). The 3 most common parenteral treatment durations were 14 days (27 infants; 23%), 7 days (18 infants; 16%), and 10 days (13 infants; 11%) (Supplemental Fig 2). Overall, 58 (50%) infants received short-course parenteral antibiotics (≤7 days), and 57 (50%) infants received long-course parenteral antibiotics. The proportion of infants receiving short-course parenteral antibiotic therapy varied by institution, with a median of 50% (range: 11%–81%). Infants receiving long-course parenteral antibiotic therapy were more likely to be ill appearing on presentation, have growth of a non–*E coli* organism, and have prolonged bacteremia (Table 1).

Outcomes

Six infants (5%) had a recurrent UTI, each diagnosed between 15 and 30 days after index discharge. Two of the 6 infants received short-course parenteral therapy, and 4 received long-course parenteral antibiotic therapy during the index

TABLE 1 Baseline Demographic and Clinical Characteristics of Infants With Bacteremic UTI

Patient Characteristics	Overall (*N* = 115)	Short-Course IV/IM Antibiotics (*n* = 58)	Long-Course IV/IM Antibiotics (*n* = 57)	*P* (χ^2 Test)
	n (%)	*n* (%)	*n* (%)	
Age ≤28 d	60 (52)	25 (43)	35 (61)	.05
Male sex	69 (60)	30 (52)	39 (68)	.06
Prematurity	10 (9)	3/53 (6)	7/54 (13)	.38[a]
Complex chronic condition	19 (17)	7 (12)	12 (21)	.19
Genitourinary anomaly	17 (15)	6 (10)	11 (19)	.18
Fever	102 (89)	51 (88)	51 (89)	.79
Ill appearance	32 (28)	10 (17)	22 (39)	.01
ICU stay	16 (14)	5 (9)	11 (19)	.10
Prolonged bacteremia	8 (7)	0	8 (14)	.002[a]
Non–*E coli* organism	22 (19)	4 (7)	18 (32)	.001[a]

[a] Fisher's exact test was performed.

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hospitalization (Table 2). There was no significant difference in rates of recurrent UTI between the 2 treatment groups (adjusted risk difference: 3%; 95% confidence interval [CI]: −5.8 to 12.7). Both infants in the short-course group who had a recurrent UTI also had a diagnosis of VUR (Supplemental Table 6). One infant in the short-course group had recurrent *E faecalis* bacteremia. This patient had grade 3 to 4 VUR diagnosed during hospitalization for the recurrent UTI and had not been receiving prophylactic antibiotics after discharge from the index hospital admission (Supplemental Table 6). Two of the 4 infants in the long-course group with recurrent UTI had grade 4 VUR and were receiving prophylactic amoxicillin at the time of recurrence. None of the 6 infants with recurrent UTI developed meningitis.

Two of the 6 infants with recurrent UTI grew an organism distinct from the causative organism isolated at the index hospitalization (Supplemental Table 6). Both of these infants had received long-course parenteral antibiotic therapy during their index hospital stay. When evaluating only those infants who had a recurrent UTI with growth of the same pathogen that caused their index UTI, there was no difference in rates of recurrence between the 2 treatment groups (adjusted risk difference: 0.2%; 95% CI: −7.8 to 8.3) (Table 2).

Fifteen infants (13%) had 30-day all-cause reutilization. There was no significant difference in the rates of reutilization between the 2 treatment groups (adjusted risk difference: 3%; 95% CI: −14.6 to 20.4). The adjusted mean LOS was significantly longer in the long-course group compared with the short-course group (adjusted mean difference: 6 days; 95% CI: 4.0 to 8.8).

Within our cohort, 67 infants were well appearing and had no known complex chronic condition, including genitourinary anomaly. Short-course parenteral antibiotic therapy was prescribed in 40 (60%) healthy, well-appearing infants. Two infants (5%) in the short-course group and 2 infants in the long-course group (7%) had a recurrent UTI.

No infants in our cohort experienced adverse events such as ICU readmission, need for mechanical ventilation or vasopressor use, or signs of neurologic sequelae within 30 days of discharge from the index hospitalization. Thirteen infants in the long-course group were discharged from the hospital with a PICC to complete intravenous (IV) antibiotic therapy. Of these, 1 infant (8%) had an ED revisit for a PICC-related mechanical complication.

TABLE 2 Outcomes of Infants With Bacteremic UTI

Outcome	Short-Course IV/IM Antibiotics (*n* = 58)	Long-Course IV/IM Antibiotics (*n* = 57)	Adjusted Relative Risk (95% CI)[a]	Percent Adjusted Risk Difference (95% CI)[a]	Adjusted Mean Difference (95% CI)[a]
Recurrent UTI, *n* (%)	2 (3)	4 (7)	1.9 (0.3 to 11.6)	3 (−5.8 to 12.7)	—
Recurrent UTI with same organism, *n* (%)	2 (3)	2 (4)	1.1 (0.1 to 8.4)	0.2 (−7.8 to 8.3)	—
All-cause reutilization, *n* (%)	6 (10)	9 (16)	1.2 (0.4 to 3.9)	3 (−14.5 to 20.6)	—
LOS, d, adjusted mean (95% CI)	4.5 (4.4 to 4.6)	10.8 (10.7 to 10.9)	—	—	6 (4.0 to 8.8)

[a] IPW was conducted by using propensity scores to achieve covariate balance in patient clinical and demographic characteristics. Marginal structural models were applied to the weighted population to obtain adjusted estimates.

DISCUSSION

In this multicenter study of young infants with bacteremic UTI, shorter courses of parenteral antibiotic therapy (ie, ≤7 days) were not associated with significantly more frequent UTI recurrence or all-cause reutilization when compared with longer courses of parenteral antibiotic therapy. Adverse events were rare in both groups, and longer courses of antibiotic therapy were associated with longer lengths of hospital stay.

A previous multicenter retrospective study by Schroeder et al[30] of infants ≤90 days old with bacteremic UTI revealed that infants with recurrent UTI did not receive longer parenteral antibiotic treatment when compared with infants without recurrent UTI in an unadjusted analysis. Similar to our study, Schroeder et al[30] reported that infants who received longer courses of parenteral antibiotics were more likely to be younger, have growth of a non–*E coli* organism in blood and urine cultures, and have blood culture positivity for >1 day. Because infants who were perceived to have higher-risk baseline characteristics received longer courses of parenteral antibiotic therapy, we used propensity scores and IPW to mitigate potential confounding by indication.

Our study had several limitations. First, despite the large number of centers included, we identified relatively few infants with bacteremia in the context of UTI. Within our cohort, rates of recurrent UTI and reutilization were low. Therefore, our analysis was not powered to capture small but potentially clinically important differences in outcomes. However, given that the incidence of 30-day adverse outcomes for infants with short-course antibiotics in our study was low, if modest UTI recurrence differences did actually exist, they might prove tolerable for

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a clinician weighing the aforementioned risks associated with prolonged parenteral antibiotic therapy.

There was also potential for misclassification in infants with recurrent UTI because patients whose recurrence was managed in the outpatient setting or at a different institution would not have been captured by using our data collection methodology. This misclassification could lead to an underestimation of the rate of recurrence. However, given the history of previous bacteremia in our cohort, our patient population is less likely to be managed in the outpatient setting when compared with infants who have uncomplicated UTI. Additionally, the overall rate of recurrence of UTI in our study was similar to that of previous studies of infants with bacteremic UTI.[30,31]

Furthermore, we could not address optimal total duration of therapy for bacteremic UTI in this study because we did not have information on choice or duration of postdischarge oral antibiotic therapy for our cohort.

Finally, it is possible that infants in the short-course parenteral antibiotic group received longer courses of oral antibiotics after discharge compared with infants in the long-course parenteral group. We were not able to evaluate for recurrences of UTI from completion of oral therapy using our data source. Thus, it is possible that a recurrent UTI that occurred 30 days after completion of oral antibiotic therapy in the short-course group was not captured in our 30-day postdischarge window.

The safety of short-course parenteral antibiotic therapy with early conversion to oral antibiotics has been established for the treatment of many invasive pediatric bacterial infections (eg, complicated pneumonia and osteomyelitis) in which prolonged IV antibiotics were previously considered the standard of care.[32,33] Prolonged courses of IV antibiotics administered via a PICC were associated with increased risk of catheter-associated complications and increased reutilization in these studies. In children who were able to tolerate oral antibiotics, parenteral antibiotic therapy did not confer a clear benefit over oral alternatives with excellent bioavailability.[32,33] However, there are limited data on the bioavailability of oral antibiotics among infants ≤60 days old. High-dose oral amoxicillin (200 mg/kg per day) has been shown to achieve therapeutic serum concentrations in term neonates with *S agalactiae* bacteremia.[34] Further investigation is needed to establish optimal dosing and bioavailability for oral antibiotics typically used to treat urinary pathogens (eg, aminopenicillins and cephalosporins) in infants ≤60 days old.

Additionally, it is possible that there is a subset of young infants with bacteremic UTI in whom longer courses of parenteral antibiotics are indicated. For instance, 4 of the 6 infants with recurrent UTI in our cohort were also diagnosed with VUR, and 3 of these infants had Grade 3 or 4 VUR. High-grade VUR is associated with an increased risk of UTI recurrence.[35,36] However, it is not known if longer duration of parenteral antibiotic therapy or longer duration of total therapy is associated with a reduced risk of recurrent UTI in infants with VUR. Future studies should focus on identifying which populations of young infants, if any, may benefit from longer courses of parenteral antibiotic therapy.

CONCLUSIONS

Young infants with bacteremic UTI who received ≤7 days of parenteral antibiotic therapy did not have significantly more 30-day recurrent UTIs or hospital reutilization than infants who received longer courses of parenteral therapy. Our data indicates that ≤7 days of parenteral antibiotic therapy may be safe in this population. Researchers in future prospective studies should seek to establish the bioavailability and optimal dosing of oral antibiotics in young infants and assess if there are particular subpopulations of infants with bacteremic UTI who may benefit from longer courses of parenteral antibiotic therapy.

FEBRILE YOUNG INFANT RESEARCH COLLABORATIVE

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ABBREVIATIONS

CFU: colony-forming unit
CI: confidence interval
CSF: cerebrospinal fluid
ED: emergency department
IPW: inverse probability weighting
IV: intravenous
IV/IM: intravenous and/or intramuscular
LOS: length of stay
PICC: peripherally inserted central catheter
UTI: urinary tract infection
VUR: vesicoureteral reflux

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Dr Desai conceptualized and designed the study, performed local data collection and data analyses, interpreted the data, drafted the initial manuscript, and reviewed and revised the manuscript critically for important intellectual content; Dr Aronson contributed to the conceptualization and design of the study, coordinated and supervised data collection locally and nationally, interpreted the data, and reviewed and revised the manuscript critically for important intellectual content; Dr Shabanova designed the statistical approach for this study, performed data analyses, interpreted the data, and reviewed and revised the manuscript critically for important intellectual content; Dr Neuman contributed to the design of the study, collected local data, interpreted the data, and reviewed and revised the manuscript critically for important intellectual content; Drs Balamuth, Pruitt, DePorre, Nigrovic, Rooholamini, Wang, Marble, Williams, Sartori, and Leazer and Ms Mitchell collected local data, interpreted the data, and reviewed and revised the manuscript critically for important intellectual content; Dr Shah conceptualized and designed the study, supervised local data collection and data analyses, interpreted the data, and reviewed and revised the manuscript critically for important intellectual content; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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